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CONSIDERATION OF CYSTIC FIBROSIS IN ADULTS, WITH A STUDY OF SWEAT ELECTROLYTE VALUES

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The sweat test used in the diagnosis of cystic fibrosis consists of the determination of chloride and sodium concentrations. In this study the sweat was collected on small cellulose sponges sealed against certain cleansed areas of skin. The test was applied to 34 persons a total of 89 times to determine its reliability. In 96 subjects assumed to be free from all known forms of cystic fibrosis, the chloride content of sweat never exceeded 70 mEq. per liter; in 6 patients with cystic fibrosis it always exceeded 75 mEq. per liter. Abnormal values of 69 mEq. per liter of chloride or 79 or more mEq. per liter of sodium were found in 8 of 25 patients with cylindrical bronchiectasis. Evidence indicates that cystic fibrosis is a general dysfunction of exocrine glands and that it should be considered among the possible causes of chronic endobronchial disease.

IN the past 20 years cystic fibrosis has emerged as a well-described and not uncommon serious illness in children. Isolated commentaries in the literature and the data herein reported suggest that cystic fibrosis may be the unsuspected cause of chronic illness in adults.

The syndrome of pancreatic insufficiency with bronchiectasis was first described by Fanconi in 1936. Two years later, after a study of 49 autopsy cases, Andersen [1] named the disease cystic fibrosis of the pancreas. Since then clinical recognition of this condition in children has become common. The disease has a variety of names, including cystic fibrosis, congenital steatorrhea, mucoviscidosis, and fibrocystic disease of the pancreas. None of these names adequately categorizes the disease.

Exocrinopathy

The primary defect in cystic fibrosis is a dysfunction of the exocrine glands, which are simple secretory structures located in the tracheobronchial mucosa, pancreas, liver, skin, salivary glands, and other organs. The common denominator in cystic fibrosis is the abnormal composition of exocrine secretions, and the manifestations of the disease seem to be directly related to this alteration in composition.[2] The mucous glands of the tracheobronchial mucosa secrete an abnormally viscid mucus that is not adequately removed, resulting in chronic endobronchial infection and airway obstruction with their sequelae. As a result, chronic pulmonary disease is the most common clinical

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manifestation of cystic fibrosis, and 90% of the deaths are due to such disease. The pancreatic secretion is abnormally viscid and gels, obstructing the ducts and resulting in atrophy of the acinar parenchyma and a variable degree of pancreatic insufficiency. In some of the biliary canaliculi the bile is precipitated in eosinophilic casts. When this is extensive it is accompanied by a severe biliary cirrhosis and portal hypertension.

Even though the sweat glands are histologically normal, an abnormal sweat is produced by patients with cystic fibrosis. The exocrine abnormality of increased salt loss in the sweat was first described by Darling and co-workers[3] in 1953. In patients with cystic fibrosis, chloride and sodium are secreted in the sweat in concentrations that are from two to four times higher than normal, and this is the most consistent measurable abnormality. The salivary glands have a variable response in this condition, while the parotid secretion has a higher than normal salt concentration, similar to sweat.

One of the outstanding features of cystic fibrosis is marked variability as to the number of exocrine organs involved and the degree of their involvement. As a result, several dissimilar clinical pictures occur. The most commonly described patient is the child with a recurrent or chronic lower respiratory infection that responds poorly to treatment and who has steatorrhea. Symptoms classically appear between 6 months and 2 years of age but may be delayed in onset or go unrecognized for many years. Nearly all of these patients have chronic endobronchial disease and most have some degree of pancreatic insufficiency, but either condition may be mild or absent. Clinical biliary disease is rare, although scattered microscopic hepatic lesions are frequently noted at autopsy. The reason for this general variability of involvement is unknown.

Of the numerous diagnostic tests described for cystic fibrosis, the determination of the sweat chloride and sodium concentration has proved the most reliable. The sweat test has been found positive in more than 99% of patients with cystic fibrosis. The only other disease proved to cause an abnormally elevated sweat electrolyte concentration is adrenal insufficiency.[4] A comparison of sweat chloride and sodium values for patients with cystic fibrosis and control groups in several studies is given in table 1. It should be especially noted that each author reports little or no overlap in the range of sweat electrolyte concentration of the control group and the patients with cystic fibrosis.

Since it appeared that age per se is no longer a contraindication to the diagnosis of cystic fibrosis, a limited study of adults for cystic fibrosis was undertaken. It was assumed that if this disease occurred in adults it would do so primarily in its incomplete forms, since no series of cases in adults has been reported. Since the sweat test has been accepted as the basic diagnostic and investigative tool for the study of cystic fibrosis, this was used as the primary method of study.

TABLE 1.—*Comparison of Levels of Chloride and Sodium in Sweat of Controls and Persons with Cystic Fibrosis*

Author	Control						Cystic Fibrosis						Method
	Chloride			Sodium			Chloride			Sodium			
	No. of Patients	mEq./Liter of Sweat Range	Av.	No. of Patients	mEq./Liter of Sweat Range	Av.	No. of Patients	mEq./Liter of Sweat Range	Av.	No. of Patients	mEq./Liter of Sweat Range	Av.	
Peterson[5]	96	4-68	34	84	8-79	39	6	79-147	110	6	58-129	99	Cellulose sponge
di Sant' Agnese[2a]	226	4-60	27	226	10-80	52	140	50-160	106	140	80-190	133	Cotton gauze
Kaiser, E., and others: A. M. A. J. Dis. Child. **92**:369, 1956	39	3-59	22	38	3-58	21	9	69-186	107	9	77-198	111	Cotton gauze
Barbero, G. J., and others: Pediatrics **18**:189, 1956	31	8-93	36	31	1-88	26	9	116-220	172	10	111-215	166	Cotton gauze
	49	6-112	37	50	1-101	37	18	103-217	162	21	102-215	163	Tube (total body)
Hsia and others[9]	83	SE† 1.3	19	83	SE 1.9	22	29	SE 4.3	101	29	SE 3.4	103	Cotton gauze
Gochberg, S. H., and Cooke, R. E.: Pediatrics **18**:701, 1956	6	10-35	16	6	11-35	18	9	51-137	80	9	42-87	79	Total body
Vink, C. L. J.: A. M. A. J. Dis. Child. **94**:40, 1957	45	5-43	20	45	5-56	21	23	79-185	118	23	78-210	121	Cotton gauze
Weeks, M. M., and Brown, G. A.: Arch. Dis. Child. **33**:74, 1958	40	6-38	22	40	7-38	21	20	50-196	111	20	36-189	104	Cotton gauze
Mauer, A. M., and West, C. D.*: A. M. A. J. Dis. Child. **92**:160, 1956	42	5-50	22				18	90-161	125				Not stated
Gibbs, G. E., and others*: Postgrad. Med. **22**:515, 1957	35	1-34	16				15	68-163	115				Not stated

* Electrolyte data estimated from graph.
† SE = standard error.

Methods and Materials

In this preliminary paper the results of sweat tests on 262 persons are reported. Subjects were selected from the following groups: patients in the Ohio Tuberculosis Hospital and the Ohio State University Hospital, patients attending several university outpatient clinics, patients with proved cystic fibrosis, relatives of these patients, selected volunteers, personnel of the Ohio Tuberculosis Hospital, and a small miscellaneous group. These tests were conducted between April 15, 1958, and Dec. 5, 1958. The subjects were selected primarily according to the medical diagnosis; the age, sex, and

race of the patients were not primary considerations in their selection. A minimum evaluation, consisting of a history, physical examination, and chest x-ray, was available for almost all subjects.

The diagnosis of cystic fibrosis was established elsewhere, and each diagnosis was verified by a review of the patient's records. All cases of bronchiectasis were documented by bronchography, and diagnostic pulmonary function studies were done for all patients with obstructive pulmonary emphysema. The diagnosis of peptic ulceration was made only after the demonstration of characteristic x-ray changes. A diagnosis of allergy was accepted only if a clinically significant antigen-antibody relationship was believed established. A diagnosis of tuberculosis was accepted only in patients with a positive culture. Similar criteria were applied for the other diagnoses listed later. Where a diagnosis was considered technically unproved but clinically sound, it was recorded as "probable" and reported separately. Serum electrolyte values were determined in 25% of tests where electrolyte imbalance was considered a possibility. Most patients were thoroughly studied, often with records extending over many years. The records on all subjects were personally reviewed, and additional laboratory studies were obtained when indicated.

The control group consisted of two sections, those persons considered to be "normal" and those with a disease which was dissimilar to all known forms of cystic fibrosis. A subject was considered normal if no active disease was found, provided any known prior illness now produced no disability. A patient was excluded from the control group if he was suspected of having any pulmonary, pancreatic, hepatic, allergic, renal, adrenal, or peptic disease.

The sweat test employed was the cellulose sponge method, which is described in detail elsewhere.[5] By this method sweat is collected on specially prepared small cellulose sponges which are sealed against cleansed skin at four standard sampling sites on the trunk. The subject, dressed in pajamas and lying on a hospital bed, is then placed in a water-tight bag which is provided with a drawstring which seals the bag around the neck. The person is then subjected to an environmental temperature of 90 F for approximately 70 minutes. The sponges are then removed, the accumulated sweat is recovered by compression of the sponges, and the samples are individually analyzed for chloride by the method of Schales and Schales[6] and for sodium by flame photometry. The average concentration of the four samples is reported for both chloride and sodium.

Results

Three hundred thirteen tests were performed on 262 persons. In 95% (249) of these persons a sufficient sweat sample was obtained to permit the direct analysis of the sweat for chloride and/or sodium concentration. The results of the tests are arranged in table 2 according to subject group regardless of diagnosis. Where more than one test was performed on a subject only the results of the first test have been included in these and other data unless otherwise stated. All chloride and sodium values are in milliequivalents per liter of sweat.

TABLE 2.—*Levels of Chloride and Sodium in Sweat of Two Hundred Forty-nine Persons, by Subject Group*

	Chloride			Sodium			
	No. of Patients	mEq./Liter of Sweat		No. of Patients	mEq./Liter of Sweat		Av. Age, Yr.
Subject Group		Range	Mean		Range	Mean	
Ohio Tuberculosis Hospital							
White	12	9.1- 56.6	33.7	13	12.7- 77.2	42.9	42.4
Nonwhite	2	17.7- 38.6	28.1	2	40.0- 53.0	46.5	39.5
Total	14	9.1- 56.6	32.9	15	12.7- 77.2	43.4	42.0
University Hospital							
White	40	3.9-129.0	31.9	36	8.1-127.0	40.4	44.7
Nonwhite	7	6.9- 39.7	20.5	7	11.0- 47.2	24.7	42.1
Total	47	0.9-129.0	30.2	43	8.1-127.0	37.5	44.3
Chest clinic (medical)							
White	34	10.6-100.4	52.7	31	16.3-125.9	61.0	55.3
Nonwhite	7	22.6- 67.5	48.9	5	27.8- 79.8	64.7	57.7
Total	41	10.6-100.4	52.1	36	16.3-125.9	61.5	55.7
Gastrointestinal clinic							
White	15	10.8- 93.0	39.7	10	6.5-100.3	47.6	50.4
Nonwhite	1	36.7	36.7	1	31.3	31.3	35.0
Total	16	10.8- 93.0	38.9	11	6.5-100.3	46.1	49.4
Allergy clinic							
White	10	12.6- 62.3	35.9	6	25.8- 80.3	44.9	50.9
Nonwhite	5	21.1- 96.1	44.0	5	19.9-112.0	53.1	24.2
Total	15	12.6- 96.1	38.6	11	19.9-112.0	48.6	42.0
Normal							
White	19	10.5- 28.5	28.5	18	11.7- 71.8	33.9	20.5
Nonwhite	0	0	0	0	0	0	0
Total	19	10.5- 28.5	28.5	18	11.7- 71.8	33.9	20.5
Ohio Tuberculosis Hospital personnel							
White	36	9.0- 64.1	37.6	32	10.9- 78.6	47.5	32.7
Nonwhite	16	11.4- 68.2	38.1	13	20.9- 78.6	43.7	35.7
Total	52	9.0- 68.2	37.8	45	10.9- 78.6	46.4	33.7
Miscellaneous							
White	8	21.1- 77.8	46.9	7	23.4- 79.2	44.9	18.2
Nonwhite	0	0	0	0	0	0	0
Total	8	21.1- 77.8	46.9	7	23.4- 79.2	44.9	18.2
Cystic fibrosis in family							
Patients and relatives all white	36	20.9-147.5	46.2	33	14.6-128.7	43.5	20.8
Total							
White	210	3.9-147.5	39.8	186	6.5-128.7	45.9	32.3
Nonwhite	38	0.9- 96.1	36.8	33	11.0-112.0	43.9	39.6
Grand total (249 subjects)	248	0.9-147.5	39.4	219	6.5-128.7	45.6	33.5

By the cellulose sponge sweat test the chloride concentration for the control group ranged from 4.1 to 68.2 mEq. per liter, with a mean of 33.8 mEq. The sodium concentration for the controls ranged from 8.1 to 78.6 mEq., with a mean of 39.3 mEq. The range of the electrolyte values in the different groups described in table 2 varied greatly, depending on the subjects comprising the group. However, for each of these groups the mean sweat electrolyte values tended to be uniform, chloride averaging 30 to 40 mEq. and sodium 35 to 49 mEq. The patients from the outpatient chest clinic (medical) had decidedly higher mean electrolyte values than

any other group, the mean for chloride being 52.1 mEq. and for sodium 61.5 mEq. There was no significant difference in the sweat electrolyte concentrations of the white and nonwhite groups. The sexes were equally represented; 52.2% of the subjects were males. The sex of the patient did not seem to influence the results. The ages of the subjects varied from 9 months to 87 years, with an average of 33.5 years.

In order to determine the reproducibility of the test, 34 persons were tested a total of 89 times. When the same person was repeatedly tested the concentration of chloride and sodium in the sweat was remarkably stable. In many subjects the results obtained by repeated examinations varied within a range of 5 mEq., and in the majority the variation was less than 10 mEq. Reproducible results of this high order were found at all levels of electrolyte concentration. The interval between the tests did not influence the data. All of the normal subjects had sweat electrolyte values within the normal range; several subjects with proved illnesses other than cystic fibrosis had abnormally elevated sweat electrolyte concentrations which were reproducible on repeated testing.

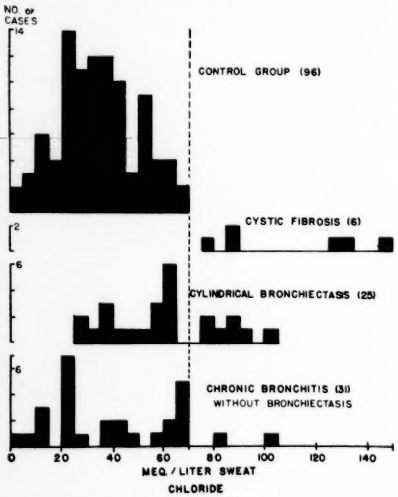

Fig. 1.—Comparison of chloride levels in sweat of controls and patients with cystic fibrosis, cylindrical bronchiectasis, and chronic bronchitis.

Normal subjects and patients with diseases dissimilar to cystic fibrosis were found to have normal sweat electrolyte values. Patients with cystic fibrosis had abnormally elevated electrolyte values. Cylindrical bronchiectasis was demonstrated in 25 patients, of whom 8 (or 36%) had an abnormally elevated sweat electrolyte concentration of 69 mEq. of chloride or 79 mEq. of sodium or more. For these eight patients electrolyte values are in the range indicating cystic fibrosis. Not all patients with cylindrical bronchiectasis had abnormal values, as is seen in figure 1. The mean electrolyte concentration for patients with cylindrical bronchiectasis is approximately double that for the control group and for groups with diseases other than cylindrical bronchiectasis. Data from the patients with cylindrical bronchiectasis yield a histogram which is intermediate between that of the control group and that of patients with cystic fibrosis (fig. 1).

Patients with chronic bronchitis without bronchiectasis have essentially normal findings. However, two patients in the bronchitis group had sweat electrolyte values that were definitely abnormally elevated; bronchograms on these patients revealed extensive bronchitis, with a variable caliber of the bronchial lumen, retained secretions, and an irregular mucosal wall. The histogram for the patients with chronic bronchitis appears to have two peaks, one that corresponds to the peak of the control group and a second similar to that for patients with cylindrical bronchiectasis. Patients with diffuse obstructive pulmonary emphysema but without cylindrical bronchiectasis or chronic bronchitis were noted to have normal findings (fig. 2). Four patients with bullous emphysema were also noted to be normal.

Of the patients with pulmonary fibrosis, four had abnormally elevated electrolyte values. Three of these patients had cylindrical bronchiectasis, and the fourth had severe chronic bronchitis with marked endobronchial changes as shown by bronchography. Patients with cystic bronchiectasis had normal sweat tests. The sweat tests were normal in those patients with pulmonary tuberculosis, cor pulmonale, arteriosclerotic heart disease, pneumonia, and osteoarthritis unless the patient also had cylindrical bronchiectasis. One patient with chronic calcific pancreatitis and diabetes mellitus had abnormally high sweat electrolyte values. Suitable studies revealed no obvious cause for the pancreatitis in this patient. Four patients with peptic ulceration had elevated sweat electrolyte values. Two of these had cylindrical bronchiectasis, while the other two patients did not have symptoms suggesting pulmonary disease. One of the latter had diabetes mellitus. One patient with bronchial asthma had abnormally high sweat electrolyte values. No additional abnormal values were found.

Normal sweat tests were encountered in numerous other conditions, some of which were cirrhosis of the liver (6 patients), cholelithiasis (5), nasal allergic pollenosis (9), "endogenous" nonallergic asthma (14), segmental or lobar chronic atelectasis (4), chronic sinusitis (8), chronic renal

disease (5), diverticulosis of the colon (5), thyrotoxicosis (3), silicosis (3), systemic hypertension (8), congestive heart failure (5), positive serology (8), otitis media (3), pulmonary sarcoidosis (4), diffuse cystic disease of the lung (1), eosinophilic granuloma of lung with diabetes insipidus (1), bronchiolectasis as shown by histopathology (1), exophthalmos (2), myasthenia gravis (1), sequestered lung (1), and malabsorption syndrome (1). There were 21 subjects with a family history of cystic fibrosis and normal sweat electrolyte values. However, subsequent studies have demonstrated abnormal sweat electrolyte values in this group, as has been reported by other authors.

Comment

Cystic fibrosis should be considered a disease that involves certain exocrine organs in such a way as to make the secretions of these organs abnormal. If the secretory abnormality is severe enough, clinical disease results. Since each organ may be involved to a variable degree, no uniform clinical picture occurs. Not only is the degree of involvement of an organ variable but also the time of onset of symptoms may vary. The majority of patients now recognized to have this disease are children with symptoms, but the patient may die during the first week of life due to meconium ileus or survive to the fourth decade.[7] In addition, some asymptomatic blood relatives of affected children have positive sweat tests, and these persons probably have a subclinical form of the disease.

The disease is believed to be genetically controlled. Past genetic studies have been based on diagnostic criteria which required the presence of steatorrhea and did not include sweat electrolyte data. A reappraisal of the genetic aspects of this disease which takes into account its generalized exocrine nature is indicated. Current genetic theories are available to meet the observed facts concerning the variability in the age of appearance of symptoms, number of organs symptomatically involved, the severity of the involvement of the organs, and apparent sporadic appearance of the disease.[8]

Currently a positive sweat test in a child with symptoms is considered diagnostic of cystic fibrosis in the absence of adrenal insufficiency. As shown in table 1, numerous investigators have demonstrated that the concentration of sweat electrolytes in patients with cystic fibrosis is considerably higher than in control groups, and the curves described by the data from these two groups have little or no overlap. Since 99% of patients with cystic fibrosis have positive sweat tests, this test has become the primary diagnostic procedure for the disease.

The data reported in this paper reveal that the sweat test is either nonspecific or that cystic fibrosis occurs in mild incomplete forms in adults. In this study of 262 subjects, 14 adult patients had abnormally high sweat electrolyte concentrations. Retesting the subjects confirmed the data, demonstrating the reproducibility of the findings. The demonstration of consistently elevated sweat electrolyte values in patients with diseases other than cystic fibrosis has not been previously reported. Ten of these 14 adults had cylindrical bronchiectasis or severe chronic endobronchial disease demonstrated by bronchography. This is the type

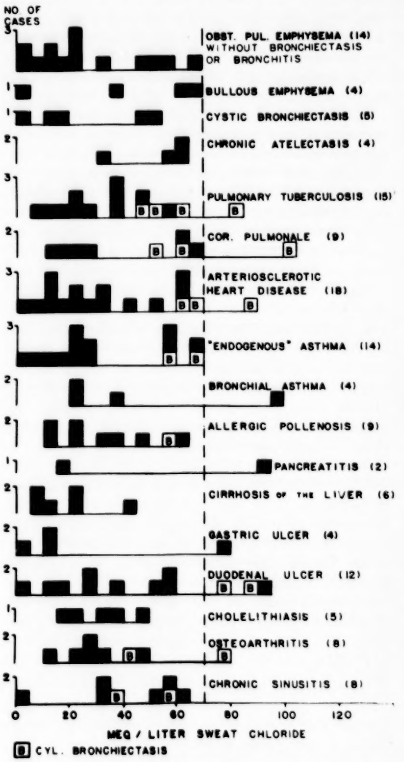

Fig. 2.—Comparison of chloride levels in sweat of subjects with various conditions, with and without cylindrical bronchiectasis.

of change that would result if stasis of secretions were the responsible factor as it is in cystic fibrosis, where severe endobronchial disease is uniformly seen as a sequela of the retention of the more viscous mucus. In the majority of adults the cause of cylindrical bronchiectasis is unknown; perhaps in some of these patients low-grade cystic fibrosis is responsible.

No common factor was noted in those patients with positive sweat tests other than diagnosis. In addition to the negative correlations already mentioned regarding age, race, sex, and time of testing, it was noted that medicaments, environment, and diet did not influence the test results in these subjects. When a patient had more than one disease and a positive test, the common factor was cylindrical bronchiectasis. That cystic fibrosis is the underlying cause in these patients with endobronchial disease because they have positive sweat tests cannot be stated from this study; however, it would appear that a relationship exists and that these patients probably have an incomplete genetic expression of cystic fibrosis.

In addition to being found in those patients with cylindrical bronchiectasis and chronic bronchitis, positive sweat tests were encountered in four other patients: two with peptic ulceration, one with chronic calcific pancreatitis, and one with allergic bronchial asthma. An explanation for this is less clear than for the group with bronchiectasis. Andersen [2b] states that peptic ulceration is a relatively frequent postmortem finding in older children with cystic fibrosis and that clinical symptoms probably due to ulcer are not uncommon in older children with the disease. Since the acid glands of the stomach are exocrine in nature, possibly they participate in the general exocrinopathy of the alimentary tract, which includes the secretions of the salivary glands, liver, pancreas, Brunner's glands, and others. A study of the gastric secretions of older children with cystic fibrosis would appear to be indicated.

The patient with chronic calcific pancreatitis and diabetes mellitus did not demonstrate any significant lung disease. Although calcification of the pancreas occasionally occurs in older children with cystic fibrosis, the usual end-result in a severely involved pancreas is "lipomatosis," which is a fibrofatty replacement of the gland without calcium deposition. Severe fatty replacement of the pancreas can exist in older children without a clear-cut history of steatorrhea or malnutrition. Since this patient did not have a detectable precipitating cause for his pancreatic disease, and since it is known that patients do have pancreatic disease without detectable pulmonary involvement, it is possible that the sweat electrolyte values in this patient were elevated due to an incomplete form of cystic fibrosis.

The final patient with a positive sweat test without endobronchial disease was a 19-year-old Negro female with bronchial asthma and a decidedly abnormal sweat test. Her chest x-ray was normal and she did not have gastrointestinal symptoms. Her family history was unremarkable, and sweat tests subsequently performed on her mother and a sibling were normal. Although cystic fibrosis is rare in the Negro, it does occur. Recently Hsia and co-workers [9] have reported a slight increase in the mean sweat electrolyte values in patients with various allergies. The race of the patient did not influence their positive results. However, the abnormal values they found apparently were not in the order of magnitude of those in this study.

In retrospect, the choice of the name cystic fibrosis of the pancreas for this disease was indeed unfortunate, since the disease is clinically primarily a respiratory illness with additional manifestations in other organs as a result of the exocrinopathy.

Summary and Conclusions

Cystic fibrosis is not exclusively a disease of children. It characteristically produces a protracted endobronchial disease, usually with additional disturbances in several exocrine organs. The sweat test is considered the best tool for the diagnosis and investigation of this disease. When this test was applied to an adult population of 262 subjects, abnormal positive tests were noted in 14 patients: 10 with chronic severe endobronchial disease and 4 additional patients, of whom 2 had peptic ulceration, 1 chronic pancreatitis, and 1 allergic bronchial asthma.

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ROENTGENOGRAPHIC AIDS IN DIAGNOSIS OF NEOPLASMS OF LIVER AND EXTRAHEPATIC DUCTS

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The histories of 35 patients with primary carcinoma of the gallbladder were reviewed in order to assess the diagnostic value of data obtained by preoperative roentgenography. The customary upper gastrointestinal series of roentgenograms showed signs of extrinsic pressure on the duodenum in 10 of 32 cases in which such a series was made. A plain film of the abdomen revealed a mass in the right upper quadrant in 3 of 24 cases. Oral cholecystography was carried out in 26 cases, 4 of which showed opacification of the biliary system. Newly developed roentgenographic techniques are helpful in selected cases and sometimes furnish decisive information. The diagnosis of polypoid growths within the gallbladder is occasionally settled by the finding of a solitary fixed filling defect on cholecystography and is an indication for cholecystectomy.

Perhaps the best way to evaluate the contribution of radiology to the diagnosis of neoplasms of the liver and extrahepatic biliary tract is to survey the various radiologic methods available for this purpose. The diagnostic yield from all clinically applicable diagnostic radiologic methods is not great, suffering badly by comparison with the high level of accuracy in roentgenographic examinations of the upper and lower parts of the gastrointestinal tract. The reason for these rather poor results is primarily the lack of a safe, simple, efficient method of effectively opacifying the liver and extrahepatic ducts.

The recognition of tumors of the liver or extrahepatic biliary system by means of abdominal plain film examination alone or in combination with gastrointestinal series, barium enema, or pyelography may frequently provide useful and even diagnostic information (fig. 1*A*).

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Gallbladder

Malignant Neoplasms.—The value of oral cholecystography depends on good liver function, and on the absence of jaundice and calcareous biliary tract disease. Its value in the diagnosis of neoplasms of the gallbladder and bile ducts is therefore small.

In an article on carcinoma of the extrahepatic biliary tract, Glenn and Hayes [1] stated, "Carcinoma of the gallbladder and of the extrahepatic ductal system, including tumors of the ampulla of Vater, has been diagnosed so rarely prior to operation or autopsy that it has received little consideration from clinicians."

Recently we reviewed the roentgenographic examinations of 35 patients who had primary carcinoma of the gallbladder. It was interesting to find that, of these 35 patients, 14 (40%) showed some detectable abnormality on one or more roentgenographic studies. Furthermore, approximately one-third of those patients who had a gastrointestinal series showed evidence of extrinsic pressure on the first or second portions of the duodenum (see table and fig. 1*B*). In a recent article on the roentgenographic diagnosis of malignant neoplasms of the gallbladder, McConnell [2] stated that about one-half of the 33 patients in his series showed evidence of extrinsic pressure on the stomach or duodenum. An appreciation, therefore, of the value of the conventional gastrointestinal roentgenographic study in the patient suspected of having a malignant neoplasm of the gallbladder may facilitate preoperative diagnosis.

Benign Polypoid Tumors.—Recently, Ten Eyck [3] reviewed a total of 2,544 cholecystectomies done at the New York Hospital in the five-year period 1952 to 1957. Preoperative cholecystograms were not available for all of the cases in which the gallbladder was examined at autopsy, but gallbladder studies were available on those cases in which there were benign polypoid lesions. In 22 cases the cholecystograms showed one or more fixed filling defects. The largest group of fixed filling defects (18 of the 22) was due to cholesterol polyps. In only one instance was the defect due to a true papilloma. In five other cases in the series of 2,544 cholecystectomies true papillomas were identified at pathological examination. These were associated with gallstones and were not identified on the cholecystograms. True papilloma of the gallbladder is a rare lesion, as was previously emphasized by Kerr and Lendrum [4] and Shepard and co-workers.[5] It has been stated that these lesions, like papillomas of the colon, are potentially malignant. Tabah and McNeer [6] reported four cases of papilloma of the gallbladder, of which three were considered to be carcinoma in situ.

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Ten Eyck found the following diagnostic points to be helpful in identifying these polypoid lesions: 1. Concentration of the contrast medium within the gallbladder is usually good. 2. The defect is smooth and either round or oval. 3. The size is usually less than 0.5 cm. and rarely greater than 1.0 cm. 4. They contain no calcium. 5. There is no change in position on repeated examinations. 6. When there are two or more defects, their relationship remains constant on repeated examinations. 7. With the patient in the upright position, there is no movement of the defect. 8. Tangential views will show the attachment of the lesion to the gallbladder wall.

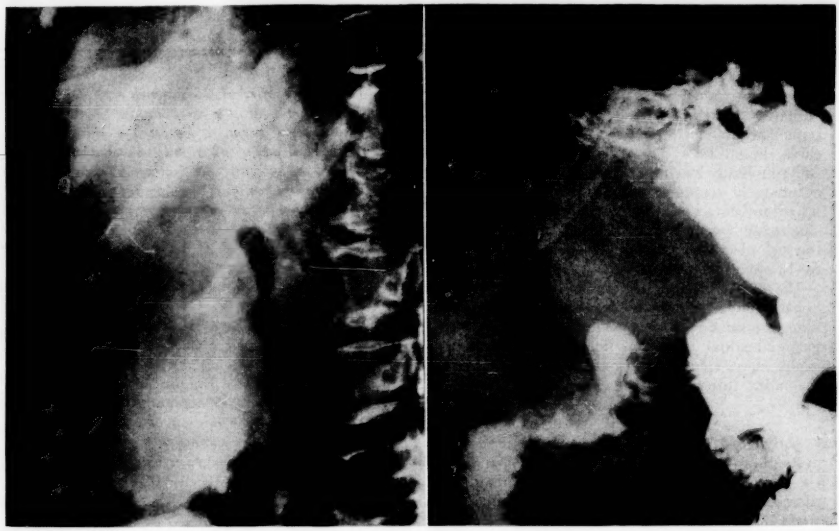

Fig. 1.—Carcinoma of gallbladder. *A*, abdominal film showing large mass in right upper quadrant indenting gas in hepatic flexure of colon. *B*, film from gastrointestinal series, showing extrinsic pressure on superior and lateral aspect of first portion of duodenum.

*Results of Roentgenographic Examination of Thirty-five Patients with Primary Carcinoma of Gallbladder**

Examination of Biliary System	No. of Patients
Oral cholecystography	
No opacification (85%)	22
Opacified	4
Intravenous cholangiography	
No opacification	2
Opacified	2
Choledocholithiasis, 1	
Dilated common duct—gallbladder not opacified, 1	
Other Roentgenographic Examinations	
Plain film of abdomen	
Noncontributory	21
Mass in right upper quadrant	3
Upper gastrointestinal series	
Noncontributory	22
Extrinsic pressure on duodenum (30%)	10
Colonic examination	
Noncontributory	25
Displacement of hepatic flexure	1
Intravenous pyelography	
Noncontributory	18
Displaced right kidney	1

*Number of patients showing detectable abnormalities on one or more of the above procedures, 14 (40%).

Finding of a solitary fixed filling defect on cholecystography is in itself adequate reason for cholecystectomy.

Bile Ducts

Cholangiography at operation or in the postoperative period has very limited value in the early diagnosis of bile duct neoplasm. Occasionally, however, operative cholangiography can be of real help in cases where the diagnosis is not immediately apparent. It is particularly helpful in evaluation of the intrahepatic bile ducts, an area not susceptible to palpation (fig. 2A). Successful demonstration of a neoplasm in the intrahepatic ductile system requires careful, precise roentgenographic technique. Insistence on a satisfactory examination will on occasion be diagnostically rewarding. In 1955 Kantor, Evans, and Glenn [7] reported their operative and postoperative experience with cholangiography. The material available for this study comprised 158 patients admitted to the Pavilion surgical services

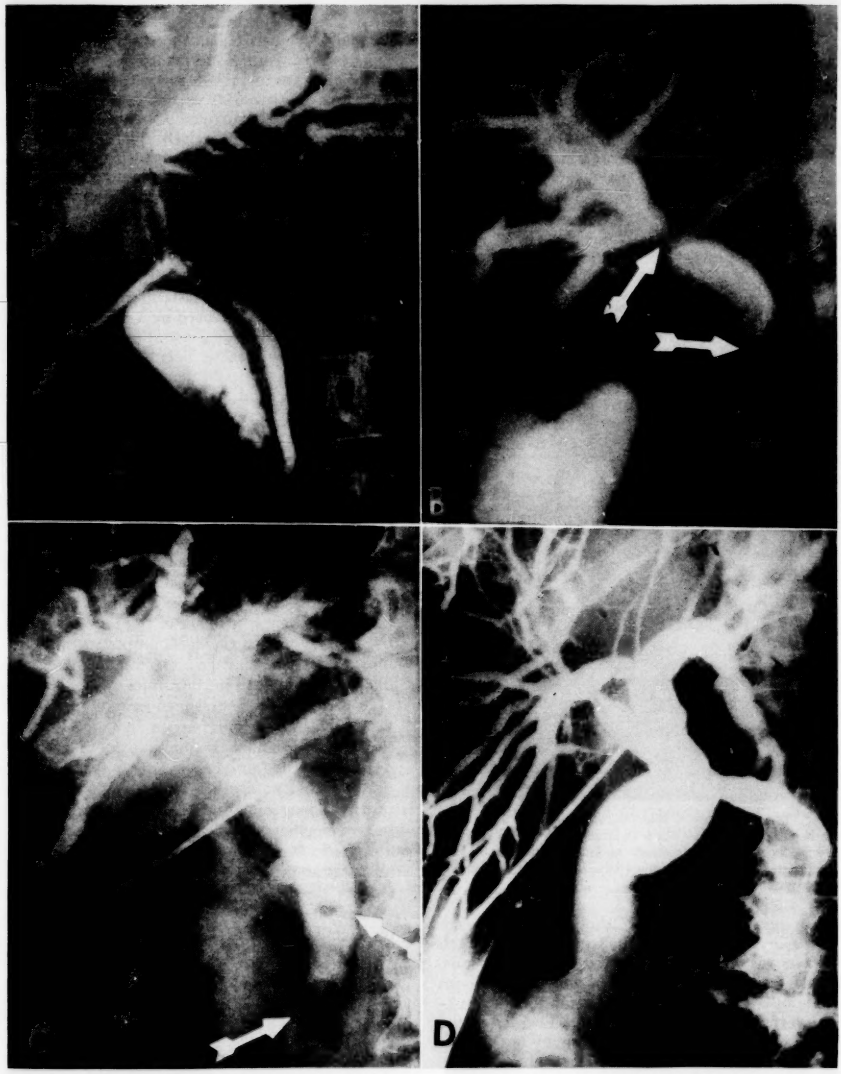

Fig. 2.—*A*, T-tube cholangiogram showing obstruction of common hepatic and right hepatic ducts by primary bile duct carcinoma. There is retrograde dilation of left hepatic duct. *B*, percutaneous transabdominal cholangiogram in a patient with carcinoma of ampulla of Vater. There is good filling of bile ducts, showing obstruction of common bile duct at ampulla (*arrow*) and partial obstruction of common hepatic duct in hilus of the liver from metastatic implant (*upper arrow*). *C*, percutaneous cholangiogram showing filling of the intrahepatic ducts and a dilated obstructed common bile duct with two stones (*arrows*). *D*, percutaneous cholangiogram showing complete filling of intrahepatic ducts, gallbladder, and common bile duct. Common bile duct is obstructed at ampulla by metastatic carcinoma from a primary carcinoma of stomach.

of the New York Hospital during the five-year period 1947 to 1952. There was some type of pathology of the biliary ducts in 116 cases. Eight cases of tumor were demonstrated (5.06%). Of these, seven (4.43% of all cases) were carcinoma.

The cholangiographic demonstration of tumor of the bile duct varies. The commonest roentgenographic appearance is the demonstration of a filling defect similar to that seen with tumors of the intestinal tract. This cannot, however, be differentiated from calculus disease. At times the picture of obstruction will be present. The differential diagnosis cannot always be made, but every effort should be made to explain all pathology demonstrated.

New Roentgenographic Techniques

Recently several new roentgenographic techniques have offered the prospect of improving diagnostic results. Two of these, intravenous and

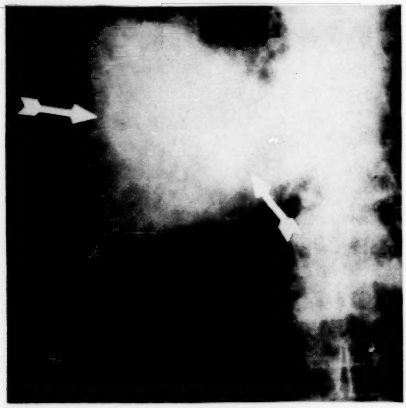

Fig. 3.—Percutaneous splenoportal venogram taken during hepatogram phase. There is large filling defect in right lobe of liver with displacement of intrahepatic portal veins (*arrows*). Patient had primary carcinoma of the stomach with large metastasis to liver.

percutaneous transhepatic cholangiography, are principally of value in visualizing the bile ducts. Intravenous cholangiography has not, in our hands, been helpful in the diagnosis of primary neoplasm of the biliary tract. It has on occasion provided useful information regarding secondary invasion of the common bile duct from cancer primary in the pancreas. In over 2,000 intravenous cholangiograms we have not demonstrated a primary neoplasm of the biliary tract system.

Percutaneous transhepatic cholangiography, first used by Carter and Saypol,[8] provides the opportunity of visualizing the bile duct system when oral or intravenous cholecystocholangiography fails. It is particularly helpful in the presence of clinical or chemical jaundice. It offers the opportunity of diagnosis prior to surgical exploration. We have found this technique to provide definitive diagnostic information in situations which otherwise might require exploratory laparotomy for recognition of the problems (fig. 2*B*, *C*, and *D*). The transabdominal insertion of a needle into the liver and the injection of a radiopaque medium, however, is not without certain risk. Our use of this technique has been restricted to the immediate preoperative period.

Liver

The clinical management of the patient suspected of having primary or metastatic disease of the liver would be greatly influenced by a diagnostic method capable of reliably demonstrating the presence or absence of such disease. Roentgenographic visualization requires opacification of the liver parenchyma. There is at present no simple, safe, completely satisfactory method of opacifying the liver. Percutaneous splenoportal venography can be used for this purpose and there has been some success with it in visualizing the right lobe of the liver. This technique is used principally for visualization of the portal venous system prior to or at the time of portacaval shunt. It provides excellent visualization of the portal vein and its intrahepatic components. A later phase of parenchymal saturation produces a hepatogram which has been found to be of diagnostic significance in tumor of the liver (fig. 3). The use of body-section roentgenography at the time of the hepatogram may be expected to increase the diagnostic yield from this type of examination.

In a discussion of roentgenographic methods of visualizing the liver, reference should be made to the use of colloidal thorium dioxide (Thorotrast). Thorium dioxide provides excellent opacification of the liver, but its use has been abandoned because of its carcinogenic effect. This, however, might not be a compelling consideration in an older person or a case in which one wants to determine the extent of metastatic liver involvement. Another disadvantage in the use of thorium dioxide is its marked toxicity to tissue, if extravasated. It is capable of producing massive desmoplastic reactions.

Summary

Examination of the gallbladder and bile ducts by conventional oral and intravenous cholecystocholangiography has proved to have little value in the diagnosis of neoplasm of the extrahepatic biliary system. In primary carcinoma of the gallbladder, the barium meal examination has provided useful information in from one-third to one-half of the cases. Solitary fixed filling defects in the gallbladder are in themselves a cause for cholecystectomy.

Operative cholangiography may on occasion demonstrate an unsuspected tumor of the intrahepatic bile ducts. Its diagnostic value is in proportion to the care and precision with which the examination is done. Of the newer roentgenographic techniques, percutaneous transhepatic cholangiography has been of demonstrated value in certain cases of obstructive jaundice. The technique of percutaneous splenoportal venography has been used to opacify the liver with encouraging diagnostic results.

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SLEEP DEPRIVATION

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and
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The effects of prolonged wakefulness were studied in a man who had been hospitalized for nervous disorders on three previous occasions. After the third hospitalization he had worked successfully under exacting conditions for six years, until he subjected himself to two periods of sleep deprivation. The first period of 89 hours precipitated an acute state of confusion from which he quickly recovered. The second period produced hallucinations, delusions, and complete disorganization. It was terminated at 168 hours and 33 minutes, but the psychotic symptoms and personality changes persisted. His affairs became confused, and he sought treatment. After four months of hospitalization he returned to work. He has been in reasonably good health for more than a year since that time.

The torture of sleep deprivation has been known since ancient times. It was used in the Spanish Inquisition no less effectively than by modern inquisitors who have employed it in their efforts to impair personality function for political reasons, as in the false confessions of "germ warfare" extorted from American flyers during the Korean war.[1] Yet we have little knowledge of the basis for the distress experienced during sleep deprivation, and there have been surprisingly few experimental or clinical studies of excessively prolonged wakefulness. With the increasing employment of drugs that influence psychological functions a burgeoning use of analeptics (ranging from caffeine to amphetamine to methylphenidate) has been seen. A brisk black market in amphetamine (Benzedrine) is known to exist. Brief psychotic reactions occurring in habitual users of amphetamine have sometimes been attributed to the direct effects of the drug, yet there is growing evidence that prolonged sleep deprivation per se may be the cause of a sweeping mental disorganization.

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A number of animal experiments have established the fact that sufficient sleep deprivation leads to brain disease and, eventually, death. However, the

neuropathological findings have been inconsistent and the cause of death remains obscure.

Sleep deprivation has been studied surprisingly little in man. In 1896 Patrick and Gilbert [2] kept three students awake for 90 hours and found decreases in sensory acuity, reaction time, motor speed, and memorizing ability; in one subject hallucinations occurred. Twenty-six years later Robinson and Herman [3] kept three subjects awake for 65 hours but found no changes in predeprivation and postdeprivation performance. Kleitman [4] deprived 35 subjects of sleep for 60 to 68 hours with the following findings: greater sensitivity to pain, normal mental and muscular efforts for short periods, irritability, occasional hallucinations, and peculiar behavioral and verbal responses. Kleitman himself remained awake for about 180 hours with the aid of amphetamine, although details of this experience are not available and it is not certain whether brief episodes of sleep occurred. Edwards,[5] on the basis of 100 hours of sleep deprivation, reported dozing, irritability, impairment of concentration and attention, difficulty in maintaining equilibrium, increasing restlessness, subjective desire to sleep, indifference, a desire to be left alone, illusions, and hallucinations. Certain extremely prolonged vigils (up to 240 hours) have been reported, which were definitely interrupted by periods of sleep and hence will not be considered here.

Tyler, alone and with co-workers,[6] reported on 350 subjects kept awake under close supervision for periods up to 112 hours. He found that blood sugar level, epinephrine-like substances in the blood, red and white blood cell concentrations, hemoglobin concentration, basal metabolism, body temperature, urinary nitrogen and creatinine levels, and excretion of 17-ketosteroids remained unaffected by prolonged wakefulness. Psychomotor performance tests showed no deterioration, provided they were not unduly long, tedious, and boring. An increase in body sway was noted. With progressively prolonged wakefulness Tyler observed electroencephalographically a decrease of alpha activity and an increase in faster activity. The psychological changes that occurred were grouped by Tyler into psychoneurotic reactions, schizophrenic-like reactions, and paranoid reactions. All reactions disappeared completely after the equivalent of a night's sleep. Tyler also found that racemic amphetamine sulfate prevented the deterioration of performance on long-duration tests of psychomotor skill.

In 1954 Lehmann and Koranyi [7] deprived six chronic schizophrenic patients of sleep for 100 hours. One of their most interesting findings was the reversion of these patients to acute symptoms which had not been present for several years. In recent studies Rioch [8] and Williams [9] have observed a large group of subjects deprived of sleep for periods up to 96 hours. They found that in general 17-hydroxysteroid levels went down during sleep deprivation and arterenol titers increased (with corresponding moderate blood pressure elevations). There was little personality change in subjects with 72 hours of sleep deprivation. From 72 to 96 hours various hypnogogic phenomena occurred. Fleeting hallucinations were noted. As the period of sleep deprivation increased, the major universal change in psychological function was a decrement in the maintenance of vigilance in certain tasks. Previously well-learned routine tasks were still well performed, and new attention-holding tasks were also well performed; however, tasks in between these two extremes showed a definite decrement. The electroencephalograms regularly showed progressive decrease in alpha activity from 100 to 80% down to almost zero. There was a return to normal in all cases in 24 to 48 hours after the resumption of normal sleep.

Bredland [10] recently found significant impairment in those activities requiring the most concentration and attention after periods of sleep deprivation up to 36 hours. Bliss and co-workers [11] have recently studied seven subjects who were deprived of sleep for 72 hours. All subjects retained the capacity to mobilize intellectual facilities for formal tests and to perform in a normal fashion, despite evidences of disorganization under informal circumstances. Subjects experienced visual distortion ranging from minor disturbances to hallucinations. Feelings of depersonalization and derealization were common. Four subjects were given 0.5 mcg. of lysergic acid diethylamide (LSD-25) per kilogram of body weight after 48 hours of sleep deprivation, and all developed hallucinations. This was half the amount previously required to produce hallucinations. The additive effects of LSD-25 and sleep deprivation have elsewhere been noted in three subjects by one of us (L. J. W.) and have also been observed by Burch.[12] Bliss and co-workers [11] also reported two clinical cases of patients with schizophrenia in whom sleep deprivation may have contributed to the precipitation of acute psychotic symptoms.

Report of a Case

At the Oklahoma Medical Center a patient has been studied who was continuously wakeful while under constant observation for more than seven days and nights in June, 1957. The setting was a radio marathon contest in which both the challenger (the patient) and the previously self-acclaimed champion were competing for the "title" and a $500 prize. Both men remained awake for 168 hours and 33 minutes, at which time the contest was declared a tie and terminated by the attending physician.

During the marathon the contestants had fairly comfortable quarters. Guards (firemen and policemen) were present at all times to observe whether either contestant fell asleep (in which case his opponent would be the victor). A doctor examined each contestant twice a day. The participants took 30-minute shifts at the microphone. From the fourth day on they received 5 mg. of dextro amphetamine twice a day. Both drank a great deal of coffee and, when not broadcasting, stayed awake by walking

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around, smoking, and conversing with friends. Abnormal symptoms were noted in both contestants from the fourth day onward. Only those of the patient who has been studied at the Oklahoma Medical Center will be reported in detail; however, the other contestant was described by the guards and by the attending physician as having shown many similar symptoms.

During the fourth day and subsequently the patient thought that various parts of the equipment were in different cities. He began to experience "memory lapses." These occurred at frequent intervals and for increasing periods until the contest was stopped. His broadcasting performance during these memory lapses was not impaired, however. Although he was inside a building the patient could not understand why there were no cars going up and down the aisle. At one point the patient saw a manikin standing by a refrigerator at a nearby exhibit in the same building and thought that it was a woman waiting to get into her car. He actually opened the refrigerator door to assist the "woman" in out of the rain. He developed the feeling that he was being punished by being made to stay awake. He accused his girl friend of kissing one of the guards, although she was in the broadcasting booth with him alone at the time. He felt that he and his competitor belonged to a secret club of nonsleepers.

During the last two days both contestants became increasingly disorganized and were often delusional. Nevertheless, they continued to force themselves to remain awake and to broadcast every 30 minutes, although much of the broadcast material was confused, disorganized, and rambling. Transient auditory and visual hallucinations apparently occurred increasingly in both subjects at various times after the fourth day. Increased suggestibility was noted to the extent that on one occasion a brief period of *folie à deux* took place, in which the delusions and hallucinations of one contestant were accepted by the other.

Because of progressively psychotic behavior, tremors, and ankle edema in both contestants, the attending physician finally insisted that the contest be brought to an end. The two contestants were taken to a local hospital. The patient was resistive and irritable. He ran out the door and was found four hours later wandering around town, an episode of which he has no memory. He was returned to the hospital, sedated, and put to bed. The following morning he signed a release and left for a week's vacation at a resort. However, he merely drove around the countryside during that week. When he returned to work he continued to have memory lapses similar to those which had been present during the contest, the last three days of which he recalled very little. His close friends observed a marked change in his personality after the marathon. He told conflicting stories about his past and seemed overwhelmed when confronted by the discrepancies. His thinking developed a bizarre flavor. He developed the delusion that he was responsible for the Egyptian-Israeli conflict and that a female secret agent in Florida was trying to get him to return to the Suez Canal zone. He used poor judgment in management of personal and financial affairs. He was irritable, restless, began to drink heavily, became tardy and irresponsible in his work, and often failed to show up at all. He was troubled by insomnia at night and lapses of attention and memory during the day.

Finally the patient's affairs became so confused that he sought hospitalization at the Veterans Administration Hospital, Oklahoma City, in September, 1957, at which time positive findings were limited to the psychiatric sphere, except for electrocardiographic changes compatible with a right bundle-branch block which had been noted for many years. There was also roentgenologic evidence of a previously noted interstitial fibrosis of the lungs. The patient was oriented in all spheres. Memory for the previous two or three days was hazy and circumscribed, with areas of amnesia. Attention and concentration were somewhat impaired. However, there was no disturbance of reasoning, judgment, abstract thinking, symbolization, or intelligence. No hallucinations or delusions were present at the time of the examination, although the patient gave a history of these occurring during the marathon. He was markedly anxious and apprehensive, and his speech was hesitant, halting, and vague. He feared that recently experienced feelings of depersonalization, estrangement, derealization, and *déjà vu* might recur. He was afraid of what he might do during one of his brief periods of amnesia, which had been taking place about once a week. His electroencephalogram was normal.

The patient's history revealed that he had been discharged from the Army in 1945 for physical reasons; however, anxiety state and emotional instability had been diagnosed at that time. His personal and professional life during the subsequent decade reflected a certain amount of instability, with three hospitalizations for nervous disorders. In November, 1956 (during a period of prolonged sleep deprivation related to night-time working conditions), he first began to experience some dissociative symptoms which were relatively mild and infrequent. In March, 1957, three months prior to the big contest, he undertook a radio marathon alone under very difficult conditions, including social isolation in a small, cramped booth. This lasted 89 hours, during which dissociative symptoms became increasingly prominent and the patient's mental state became progressively confused. On receiving sedation and a night's sleep the patient recovered from the acute symptoms, but he had "memory lapses" lasting 20 to 30 minutes several times during the three-month interval preceding the record-breaking marathon previously described.

In the hospital the patient was assigned to occupational, recreational, and group therapy and was in addition seen twice a week in psychotherapy. He responded rapidly and showed marked improve-

ment. During his hospitalization of four months he had only one dissociative reaction, a short fugue in which he wandered off the ward with subsequent amnesia. After his discharge from the hospital in January, 1958, he returned to work and has remained in reasonably good health since that time.

Comment

It has already been established that sleep deprivation brings with it an increasing burden of drowsiness (subject to diurnal variations) [4] and brief lapses of awareness or "microsleeps." [13] The findings in this case suggest that acute, prolonged sleep deprivation inevitably produces a delirious reaction in which contact with the environment becomes progressively impaired, and latent psychopathological trends become exaggerated. The dissociative symptoms which became so prominent in this case had already manifested themselves before the present illness. Despite his preexisting emotional instability, however, the patient had functioned at an adequate level, remaining out of the hospital and earning a good living for six years prior to admission.

His first "memory lapses" occurred at a time when he was working long hours and suffering from chronic lack of sleep. In March, 1957, with the added stress of discomfort and isolation, the patient developed more rapid disorganization and was confused at the end of 89 hours of sleep deprivation. Although acute symptoms quickly subsided, this episode was followed by an increased frequency of "memory lapses." During the long marathon in June, 1957, under conditions that were more favorable and where isolation did not play a role, bizarre behavior did not occur until the fourth day of wakefulness. In the fifth, sixth, and seventh days there was a progressive emergence of psychopathology with illusions, hallucinations, delusions, depersonalization, *déjà vu*, derealization, disorientation, and confusion. The occurrence of such a dream-like state in persons habitually deprived of sleep, with the apparently inevitable develop. ent of hallucinations, is not fully understood. A theoretical explanation has been offered elsewhere.[14]

Of particular interest in this case is the persistence of marked personality changes for a period of many weeks after the seven days and nights of sleep deprivation. Poor financial judgment, increased frequency and severity of "memory lapses," impulsive behavior, tardiness and irresponsibility in getting to work (compared with previously demonstrated compulsive punctuality), and paranoid ideation were present over a period of three months and represent an exacerbation of preexisting psychopathological tendencies, some of which were merely latent. The degree to which sleep deprivation per se was responsible for this more chronic syndrome cannot be ascertained, but there is little doubt that it contributed. These observations should remind us of the ways in which different kinds of stress may exert an additive disrupting effect on personality integration. Sleep deprivation, along with other factors, may contribute to the emergence of significant psychopathological symptoms in persons whose personality integration might be sustained if normal amounts of sleep were provided.

We have referred to the regular use of sleep deprivation in the elicitation of false confessions for political reasons in police states. Careful scrutiny of the data available in individual cases suggests that such confessions may have been made during periods of psychosis induced (at least in part) by prolonged wakefulness. The restoration of normal ego functions through subsequent good treatment may leave the victim of such a maneuver at a loss to account for his actions. Under such circumstances he may rationalize, excuse, or even defend his behavior on many grounds other than the true ones, which he could not be expected to comprehend.

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RESPIRATORY DISEASE OF MUSHROOM WORKERS

FARMER'S LUNG

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Clinical observations of 16 patients were collected to exemplify a possible new disease entity. Each was a Puerto Rican migratory worker engaged in the handling of compost used as soil for growing mushrooms in Pennsylvania. The disease has not, as yet, been observed or identified in other persons. Immunity was not conferred by a single episode or successive episodes. The disease recurred with reexposure. Treatment was nonspecific and supportive. Removal of contact from the compost was necessary for cure. The consistent findings were respiratory signs and symptoms, characteristic roentgenographic appearance of lung fields, eosinophil count elevation, nationality of patient, and contact with the compost. The natural pattern of the disease resembles that of "farmer's lung" and "silo-filler's disease." The etiology remains undetermined.

Diffuse infiltrations of the lungs seen by us in the x-ray department of Chester County Hospital during the past two years in migrant Puerto Rican workers posed some diagnostic problems. Our hospital in West Chester, Pennsylvania, is in the heart of one of America's centers of commercial mushroom culture. Native workers are periodically augmented by migrant Puerto Ricans, who seem to be susceptible to some substance in the compost beds used in growing mushrooms which does not affect the workers of local origin. These lung changes resemble farmer's lung, as described by Campbell in 1932,[1] and the ailment referred to as "thresher's lung" by Törnell.[2] The histopathology of this illness has not been extensively documented,[3] and while the etiology is obscure there seems to be a connection with the inhalation of products of moldy or spoiled hay.[4] Another syndrome like farmer's lung, called silo-filler's disease, also has features in common with those found in our survey, but the causes are said to arise from the inhalation of nitrogen dioxide emanating from fermenting silage.[5] Frank [6] has done an excellent review of the subject.

Clinical Manifestations

This syndrome might be divided into an acute and chronic phase. The acute phase usually subsides rapidly within one to six weeks after the patient is removed from exposure. Immunity seems to be almost absent since recurrence of acute symptoms appears with each fresh exposure. Recurrent attacks with repeated exposures seem to be mild in some patients, and these are the only "chronic" types we encountered.

Symptoms and signs occurred with decreasing frequency, as follows (see table): cough; rales; pain in chest, epigastric area, or muscles; dyspnea; yellow or greenish yellow sputum; nausea and vomiting; headache; chill; rapid weight loss; anorexia; sore throat; night sweat; malaise; diarrhea; hemoptysis; and epistaxis. A combination of symptoms often suggesting tuberculosis was observed, and in spite of their sputum being free of tubercle bacilli five patients were actually treated for tuberculosis, two of them for three months, before the physicians were convinced of their diagnostic error.

From the Department of Radiology, Chester County Hospital.

Only three patients were tested for tuberculin reactions and all gave positive results. Five patients had repeated hospital admissions and one was treated four times within a period of 14 months for attacks of acute respiratory symptoms.

Patients' temperature elevation was marked during the acute phase, often reaching 104 F (40 C), usually with diurnal variations. Tachycardia was commensurate with the intensity of fever. The white blood cell count averaged 12,000 per cubic millimeter and in one case was 25,000. Among all the patients the eosinophil counts varied from 2 to 10 and averaged more than 4% per cubic millimeter. Remission of symptoms usually coincided with hospitalization. Antibiotics were used routinely, but their value in treatment of this disease has not been established.

The average duration of an acute attack was 22 days, but it varied from 4 to 46 days. Similar duration of symptoms occurred in the recurrent acute attacks, but with less intensity. Two patients had symptoms for three to six months, but during this interval they worked intermittently. Only one patient was followed up for 15 months, with slight

improvement in spite of protection from additional exposure to compost beds. Since all of these Puerto Ricans were migratory workers they were not available for a longer follow-up period.

*Frequency of Clinical Symptoms of Mushroom Worker's Disease in Sixteen Puerto Rican Patients**

Symptoms	No. of Patients
Cough	15
Rales	13
Pain (chest, epigastric, substernal)	12
Dyspnea	10
Sputum (yellow or greenish yellow)	8
Nausea, vomiting	7
Headache	7
Chills	6
Weight loss	5
Anorexia	4
Sore throat	4
Night sweats	4
Malaise	4
Diarrhea	2
Hemoptysis	1
Epistaxis	1

*All patients were in their early 20's except six in their 30's and one aged 46.

Roentgenographic Findings.—Nothing pathognomonic was noted in the roentgenographic findings of patients in this group. Usually the infiltrations were diffuse, often suggesting the picture of azotemia; rarely were the lesions regular in outline (fig. 1). The patient in figure 1 had had pain and coughing for five days and then experienced chills and fever. On the day of admission he had nosebleed, shortness of breath, loss of appetite, and headache. His temperature was 103 F (39.4 C), and his pulse rate was 132 per minute. There were bilateral rales, increased tactile fremitus, and dulness at both bases.

Diffusely scattered minute seedings, when seen, were seldom confluent and consolidative. Occasionally the infiltrations were predominantly segmental, and when this occurred in the upper lobes tuberculosis was considered in the differential diagnosis. Only twice was the appearance similar to silica pneumoconiosis. Bronchopneumonia, bronchitis, bronchiolitis, lobar pneumonia, tuberculosis, and silicosis were the diagnoses offered by the radiologist when the first few cases were encountered (fig. 2). The 46-year-old man in figure 2 had been in the United States for only six weeks. He was admitted to hospital complaining of night sweats, fever, chest pain, and shortness of breath. His temperature was 99 F (37.2 C) and pulse rate 100 per minute, and bilateral crepitant rales were found.

After appraising the history of exposures to mushroom compost which usually occurred in the spring and autumn when active handling of compost is apt to occur, the common disease syndrome in these patients came to be recognized. The roentgenographic findings changed rather rapidly after the patients were admitted to the hospital and put under active treatment. Resolution of the pulmonary infiltrations was rapid at first but lagged after subsidence of the clinical symptoms. Resolution usually took place within a matter of days, seldom later than two weeks. In the chronic cases resolution was slower and was measured in months.

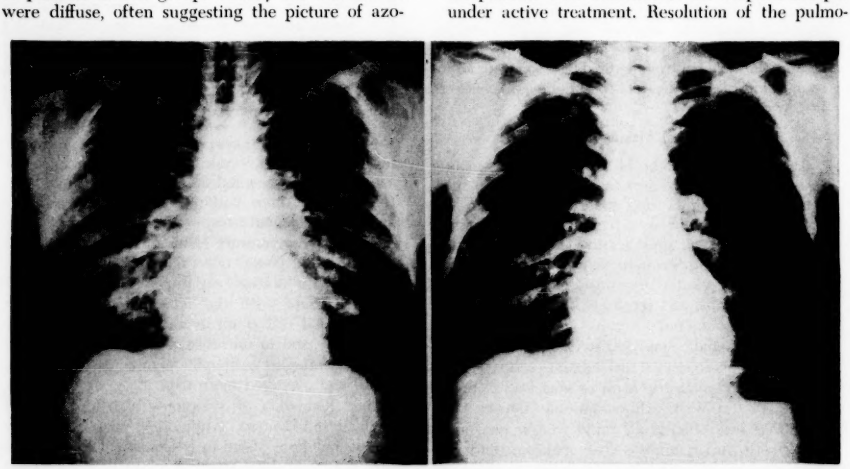

Fig. 1.—X-ray examination on admission (*left*) revealed extensive diffuse infiltrations in both lungs; reexamination 13 days later (*right*) showed almost complete resolution of pulmonary infiltrations.

Comment

All patients seemed to react acutely to exposure, usually within a matter of hours, either when they were laying down freshly "pasteurized" compost or when raking and moving old compost heaps. In most of the patients the initial cough, feeling of chest constriction, and shortness of breath were not incapacitating, so that many days elapsed before the symptoms were severe enough to warrant hospitalization. Fever, cough, and pain were the symptoms on admission of the patient to the hospital. At this phase of the disease the roentgenographic findings were apt to be definite, if not already past the full-blown phase. In the chronic cases the symptoms suggested chronic bronchitis and the roentgenographic findings suggested the presence of increased fibrosis. Bronchiectasis was found in one patient.

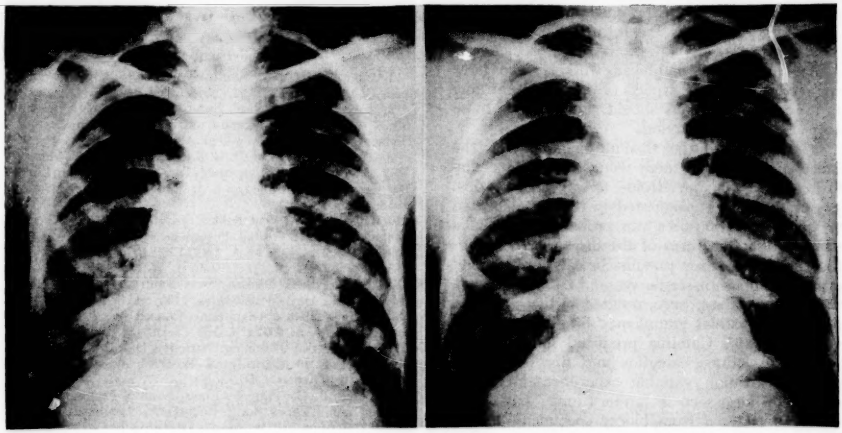

Fig. 2.—Admission x-ray examination (*left*) revealed diffuse infiltrations; reexamination 37 days later (*right*) showed that almost complete resolution had occurred, although the patient was then symptom-free.

Sputum examinations done in every instance failed to reveal a definite causative agent. Other observers also have been unable to assign an etiological factor to this entity. Dr. George Truitt in our hospital found skin reactions to Candida in three patients whom he tested.

In most reports concerning farmer's lung it is presumed that the offending agent in moldy hay is either fungus, spores, or other organic components. When discussed under the name of silo-filler's disease the hazard is presumed to originate from certain gases, especially nitrogen dioxide, liberated in recently filled silos. One part of this gas to 10,000 of air is known to be dangerous even for short exposures, while 2½ parts per 10,000 is a fatal concentration. Nitrogen dioxide is one of the most insidious of all toxic gases, and one may inhale its vapors in small amounts without having immediate ill-effects; but before many hours have elapsed edema of the lungs may develop and the victim drown in his own body fluids which have poured out into his lungs.[6] The description of this syndrome is not unlike that involving our patients. In the mushroom industry when compost is being prepared for seeding it is pasteurized by the introduction of live steam which gives the bed an average temperature of 150 F, and this is maintained for five days. Then the damp compost of horse manure and the straw of wheat and barley, at a temperature of 70 to 80 F, are laid down on tiers of platforms about 15 in. above each other. The buildings are about 15 ft. high, 40 ft. wide, and 120 ft. long, and ventilated only through a door at either end of the dark shed.

It is possible that some of the gases which collect above the beds contain small quantities of nitrogen dioxide, especially since strong reducing conditions are present. Since nitrous acid is very unstable, it will break up into nitric oxide and nitrogen dioxide quite easily. Nitric oxide is highly volatile and may escape from the compost beds with carbon dioxide, but when it comes in contact with air it reacts with oxygen to form the heavy nitrogen dioxide gas. This is the lethal gas which emanates from burning x-ray films.[7]

The steaming compost beds which are laid down initially become drier as the mushrooms grow, and after harvesting the surface of the beds is covered by a thick white mold. Before these old beds are cleaned out, however, they are first hosed down

with live steam so that one would expect less organic dust to rise than would otherwise occur. In this connection it is interesting to note that only 2 of the 16 patients contracted their illness during this phase of their occupation, while the other 14 patients became ill when they were laying down the fresh compost beds.

In spite of claims to the contrary we cannot make a sharp differentiation in reviewing the literature between the syndromes of farmer's lung and silo-filler's disease, and the symptomatology of our patients could fit either. While we believe that nitrogen dioxide might be an initiating factor, we would admit the possibility that organic dust might also be an exciting agent.

In the Chester County area of Pennsylvania it is estimated that about 75% of the workers in the mushroom industry are migrants, usually Puerto Rican. Why they should be more susceptible than workers recruited from the neighborhood to acute respiratory disease on exposure to compost beds is not apparent. It is curious that foremen and other permanently employed workers who have engaged in the same aspects of mushroom farming as the migrant workers should have escaped these acute respiratory reactions.

If organic dust rather than nitrogen dioxide is the cause of symptoms, there would be no objection to regarding this syndrome as an organic dust pneumoconiosis as suggested by Frank. Repeated or prolonged exposures can probably result in a chronic disabling form of the disease and so further stimulate silica pneumoconiosis. Zettergren [8] exposed rabbits to sterile rye and oat dust which, after five days' exposure, resulted in the formation of small interstitial granulomas. Similar dusts contaminated with Candida produced lesions which seemed to induce caseation and fibrosis. Except for the caseation variable experimental changes similar to those seen in farmer's lung [9] have been found in material from biopsy specimens.

Summary

During the past two years 16 cases of respiratory disease were encountered among migrant Puerto Rican workers in the mushroom industry in and around Chester County, Pennsylvania. The etiology of this disease is not known, but symptoms arise during the bedding down or cleaning out of damp compost beds which contain moldy hay and silage, among many other organic products. Patients seem to develop a prompt response to exposure, which, if sufficiently intense, can cause dyspnea, nausea, vomiting, pain, cough, sputum, fever, tachycardia, and prostration. The symptoms subside with removal of the patient from contact with the agent.

The roentgenographic appearance of the lungs suggests widespread diffuse infiltrations; isolated lesions when seen are small or minute, irregular in outline, and occasionally confluent. Resolution is rapid in the acute stages; increased fibrosis is encountered in the chronic stage. The clinical and roentgenographic findings in this group of cases are like those described in farmer's lung and, in many respects, also like those in silo-filler's disease.

Drs. Asa Potts and George Truitt and Mr. J. Boyd Gentry furnished data pertinent to this study.

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CAUSE AND TREATMENT OF ORNITHOSIS.—Some 100 species of birds, of which more than half are psittacines, have been found to be infected with the psittacosis-lymphogranuloma group of organisms; the infection of poultry has recently been recognized as a public health and economic problem. Mammalian reservoirs of the disease have also been noted, but so far few human infections have been attributed to this means of spread. Broad-spectrum antibiotics are very effective in the treatment of the disease in man, while experimental feeding and injection of parakeets with tetracycline compounds have shown good results.—Zoonoses, *WHO Chronicle*, May, 1959.

INTERNATIONAL COOPERATION IN POSTGRADUATE MEDICAL EDUCATION WITH REGARD TO INDIA

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Higher education in the science and practice of medicine has become an endeavor which can hope to succeed only if it can reach across national or regional boundaries. Since World War II many areas in the world have emerged as newly independent political units. The invigorating breath of real freedom has aroused these people and triggered a chain reaction of unprecedented vigorous activity in these new nations. Their task, however, is colossal. Expert planning and careful decisions on priority are needed. Problems threatening the mere continuance of existence must take priority over the urge for better standards of education or of better amenities in life. Under the circumstances it is inevitable that all underdeveloped countries face a severe shortage of trained men and of efficient tools in all fields. Before they can raise their level to self-sufficiency, even in minor things, they cannot but depend on help and cooperation from the better-placed members of the free world. Medical education in general, and postgraduate medical education in particular, is one such area which, in spite of its recognized importance for world health, cannot get top priority in an area which suffers staggeringly low levels of food, clothing, and shelter.

As a member from one such nation, struggling to avoid being coerced into wasteful violent pursuits and to raise its standards of life, I must call attention to these realities and voice our great hope and faith in the free world for international cooperation in the matter of postgraduate medical education. I cannot begin this presentation, therefore, without a sincere compliment to the vision of international agencies such as the Rockefeller Foundation, which has sponsored my visit, and the World Health Organization, the Technical Corporation Mission, and the Colombo Plan, which have already contributed so much toward medical research and education in underdeveloped countries. We have gained through this experience a much better and clearer understanding of the problems which face us in postgraduate medical education. It shall be my effort here to record some of these problems and to explore the ways to meet them. You will pardon me, if the examples I cite are from areas where I work.

Professor of Pharmacology, Seth G. S. Medical College, Parel, Bombay.

Read before the Second World Conference on Medical Education, Chicago, Aug. 30-Sept. 4, 1959.

This paper and the three following papers conclude the presentations at the First Plenary Session. The other four papers presented at the First Plenary Session appeared in the Aug. 29 issue of THE JOURNAL.

Need for Trained Teachers

A major problem in postgraduate medical education in India stems from the rapid increase in the number of medical schools. In 1926, we had 10 medical schools. In 1947 our country was partitioned and by 1949 Free India had created 13 new medical schools to help meet the demand for more doctors. This demand persists and today we have 50 medical schools; by 1965 this number is planned to be raised to 67. The drug industry has also awakened to much greater activity and a number of cooperative international combines have started their plants in India, creating a significant demand for persons qualified for medical and scientific work.

The consequent increase in our educational requirements presents many important facets. A number of these call for international help and cooperation. A major one concerns teacher training. We have an acute inadequacy of medical teachers so that our departments, especially the preclinical ones, are headed on the one hand by men long beyond their age of superannuation or on the other hand by young teachers before they are sufficiently mature for the task, while many teaching posts remain vacant. In clinical subjects the problem is further complicated by the enormity of the outpatient and inpatient hospital work which has to be tackled by the personnel before they can attend to any teaching or research. Moreover, in many schools there are only part-time or visiting clinicians and the situation is still worse. Great efforts are being made to establish full-time clinical departments but with only indifferent success. There is a general shortage of doctors, and, as everywhere, teaching careers are not financially attractive. For example, at my school in Bombay, before the Rockefeller Foundation extended its help we could not plan our full-time medicine and surgery departments. Thus, there are many schools and not enough teachers.

This situation has created a peculiar demand on our postgraduate training programs. Particularly in preclinical subjects, it is expected that every postgraduate student, a few years after his training, will automatically be able to head a new department. In our postgraduate educational need, therefore, apart from the accepted dictum that a candidate should be encouraged to work on a problem of his own interest, it also becomes necessary to interest him further in the methodology and the techniques of the subject as a whole.

Role of International Cooperation

For any effective fulfillment of these requirements, we must for the most part invoke international cooperation. Only those departments which already maintain a broad research interest and follow a virile educational policy can fairly be charged with this task, if adequate standards are to be attained. Most of our postgraduate students therefore aim and hope to be sent abroad in order that they may obtain intensive firsthand experience of working with a dynamic team of teachers and also broaden their outlook by the experience of traveling abroad. Recognition and comprehension of this by our colleagues abroad is vital. I shall return to this point later.

In the matter of adequacy of research equipment international cooperation has been our mainstay, and it will continue to be so for some years to come. Let me therefore not labor this point. Rather, I would stress the great need of institutional workshop facilities and technician training programs on a nationwide basis. It will astonish some of you to know that workshop facilities are not available to every medical institute in India. The effects of this want are too obvious to need discussion.

International help and cooperation evidently has an important role today in our efforts to meet the varied requirements of postgraduate medical education. Fortunately, the existing international agencies have already well-laid-out channels for international cooperation and a variety of forms of this cooperation are also well known. Visiting professorships, teacher exchanges, fellowships, and travel grants are some of them. I have already referred to equipment gifts. These may be made available either through (*a*) private funds, such as the Rockefeller Foundation and the Ford Foundation; (*b*) business corporations; (*c*) universities establishing cooperative relations with universities of other countries with mutual benefit; and (*d*) international organizations, such as the World Health Organization, the Food and Agriculture Organization of the United Nations, and the United Nations Educational, Scientific, and Cultural Organization.

I would like to quote certain advantages attached to help available from private foundations such as "(1) flexibility of programme, (2) capacity to make commitments over a considerable period of time, (3) comparative freedom from political complications and (4) ability to support search for knowledge without undue regard to short time practical results." International cooperation, keeping in mind the above considerations, will help a long way to solve this enormous problem.

Specific Needs in India

Experience regarding visiting professorships to countries like India deserves study. The impressive work done by visiting professors in India, Burma, Malaya, Egypt, and elsewhere has gone a long way toward stimulating medical research activities among the younger staff members of the institutions visited. While this general awakening is of great importance, it is nevertheless true that if our objective is to develop institutions, department by department, so as to equip each for postgraduate educational responsibilities, it has to be admitted that much remains to be desired. Now, it has to be admitted that full professors from the United States, Canada, United Kingdom, etc., cannot be blamed if they are not eager to spend as much as a year or two in India. Yet, if it is the full growth of a department which we desire, nothing less than a full professor with maturity as an academician and experience as a head of the department and postgraduate teacher is needed to organize and develop the required spectrum of activity in a department so that it can undertake postgraduate training in a variety of aspects of the particular discipline. This is not easy.

The idea therefore of exchanging teachers is more practicable and perhaps more profitable. It has to be a true exchange of teachers, however, each man giving his place to the other so that the experiences from the same department are discussed and exchanged over the entire period on a person to person basis. In fact I would even suggest that the Indian counterpart should continue in his exchange department for two to three months after his exchange teacher has returned.

Fellowships of short and long duration have been in vogue for sometime. In view of the probability that fellows trained under these programs are liable on their return to be charged with postgraduate education, a revision of their training program abroad seems indicated. There is much in favor of the current practice of encouraging fellows to desist from routine course work toward degrees and to concentrate on some good research activity. It is also necessary, however, that the fellow does not confine himself exclusively to one kind of work but also in addition obtains experience of all the current activities—teaching and research—in the department where he works.

May I make another suggestion which concerns the biological aspect of medical sciences? In India postgraduate students in physiology and pharmacology are as a rule medical men, so that postgraduate education in these disciplines is almost exclusively medical in motivation. Little is easily appreciated, therefore, of the broad biological spread of these disciplines. It should prove interesting to place some medical postgraduates in exclusively nonmedical laboratories and institutions for a portion of their fellowship. The work problems would, of course, be the same or similar but a different or broader perspective is likely to be obtained from such environmental changes. The Institute of

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Biology at Cambridge under Professor Gaddum, Chelsea Polytechnique Institute, London, and the Marine Biological Laboratory at Woods Hole, Mass., are the kind of places which are in my mind in this connection.

All fellowships, travel grants, etc., are most effective when they are so timed as to meet a crucial phase in a person's professional career—when he needs an extra stimulus or assistance, to move him beyond the limits of his formal training or the confines of departmental circumstances. It is a common experience that a young man works sincerely for some years after his return from a fellowship abroad, only to find himself slowed down, if not "spent up," in the organizational base work of his new department. Yet it is at this stage that he best appreciates the little gaps between the foreign training he has received as a young man and the local requirements he has appreciated anew from active experience, and it is also at this stage that he can really comprehend his professional needs for the future. A return visit abroad even if for a short period at this stage pays rich dividends. I would urge, therefore, that our fellowship programs should from the very beginning of the project be considered a two-stage operation.

One important aspect of postgraduate education on the clinical side is setting up of a well-planned residency training program. This has not been possible, even though its importance is well realized, due to lack of funds to pay and house the trainees—help of international cooperation is urgently needed in this direction.

Equipping the increasing number of our medical institutions with adequate library facilities and audiovisual aid equipment is another task which can only be undertaken with international help and cooperation.

I have spoken mainly of our peculiar problems in postgraduate medical education in India. I have avoided discussion of problems common to all, such as (1) selection of, and incentives to postgraduate students, (2) training methods and programs, and (3) medical versus nonmedical training in basic medical discipline.

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INTERNATIONAL COOPERATION IN POSTGRADUATE MEDICAL EDUCATION IN MALAYA

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The cessation of hostilities in southeast Asia in 1945 imposed serious problems in the medical rehabilitation of my country. Some of the more grave issues involved were the considerable depletion of senior and experienced teachers and medical specialists in the university and government medical services as a direct result of the war. The enforced closure of the medical school during the period of hostilities and enemy occupation for a period of five years added seriously to the problem of an acute numerical shortage of doctors for the whole country, while damage and destruction of hospitals and other buildings during the war aggravated the problem further.

The gigantic task of rehabilitation was faced with the twin problem of producing more doctors, teachers, specialists, and research workers and the construction of more hospitals and the repair of damaged buildings, both of which were tackled with eagerness and determination. The problem of rehabilitation was greatly complicated by the inevitable changes which wars have always brought about. The changing political pattern from a colonial to an independent self-governing status, the awakening of national and political consciousness of the people recently liberated from enemy occupation and oppression, the natural aspiration of the citizens to get the top posts in medicine and the other public services of the country, previously barred to them by the rapid "Malayanization" of the medical and public services, and the consequent staggering and eventual cessation of recruitment of specialists and senior consultants into the medical service of Malaya by the colonial office in London were some of the complicating factors which added to the difficulties of medical rehabilitation.

I am sure I am expressing the gratitude of my country for the help and encouragement we have

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Address to the First Plenary Session of the Second World Conference on Medical Education, Chicago, Aug. 31, 1959.

received from international cooperation in our national effort. We have, on our part, doubled the intake of undergraduates into our medical school, so as to produce more doctors for the country. We have also recruited doctors from India, the United Kingdom, and the other Commonwealth countries to meet the shortage of medical personnel. We have recruited medical specialists and dental specialists from overseas where no local candidates are available to fill the important posts. We have increased the number of scholarships and fellowships a hundredfold to enable our medical and dental graduates and nurses to go to the United Kingdom, the Commonwealth, to the United States, and to Europe to study and to do research so as to equip them with the knowledge and experience to return as specialists and teachers in the various fields of medicine, dentistry, and nursing.

Development of Postgraduate Medical Education Program

The University of Malaya, conscious of the importance of postgraduate medical education instituted, with the assistance from the World Health Organization who supplied teachers and fellowships, a diploma course in public health for graduates from Malaya and from southeast Asian countries. The course has been in existence now for five years and its importance in providing men and women trained in the principles of preventive medicine and public health in a rapidly developing rural and industrial area is beyond measure.

In order to assist in this program of postgraduate medical education, the Colonial Development and Welfare Fund of the United Kingdom contributed a major share in the cost of the construction of the magnificent building of the Institute of Health where undergraduates and graduates in medicine and nursing are trained in the principles and practice of public health and social medicine.

Through the assistance of the Colombo Plan and with the cooperation of the Postgraduate Medical Federation of Australia, eminent and experienced teachers from Australia are being sent regularly by the Royal Australasian College of Surgeons to teach and examine at the faculty of medicine, and the teaching hospital at Singapore has graduates specializing in many fields of surgery.

The China Medical Board has made several handsome contributions for the development of a first-class medical library housing 70,000 volumes and 600 international medical journals and the purchase of much-needed and valuable equipment and apparatus for basic research in the preclinical departments of the medical school.

The Colonial Development and Welfare Fund of the United Kingdom has helped us to build a new and imposing department of pathology and museum to assist in research and teaching. The nursing school, too, has increased its intake of admission for the nursing profession. In this school, the government and university specialists assisted by a team of World Health Organization tutors have developed a number of postgraduate nursing diplomas, such as ward administration, pediatric training, orthopedic nursing, psychiatric nursing, and tuberculosis training, so that more girls are obtaining their postgraduate diplomas in the country and fewer are going overseas to the United Kingdom and the Commonwealth for their postgraduate education.

The medical school has also been assisted by visiting professorships in parasitology, and a visiting professorship in pharmacology is being arranged with the China Medical Board at this moment.

Methods of International Cooperation

It might appear to be a curious fact that, while international jealousies and national monopolistic tendencies were and indeed are prevailing throughout the world, international cooperation in medicine has been a feature which must have puzzled the orderly thinking of many a philosopher.

Outstanding among these could be mentioned the wide and easy dissemination of scientific discoveries within and without countries, whether they were at war or at peace or whether they were racially or otherwise on friendly terms. Even more outstanding, perhaps, has been the effort at international cooperation and, indeed, control for the prevention of entry of disease from one country to another. Talent, wherever it exists, has been recognized by medicine without fear or favor, and it has borrowed abundantly from these sources.

Developments, particularly during this century, have contracted the world almost to insignificance. Today, one does not have to face the challenge of a hazardous journey of a few thousand miles as did our forebears. These developments have naturally tended to bring persons of eminence, of wisdom, and of knowledge in contact, one with the other, and so have enabled more liberal and intimate discussions on which a basis for future development, future programs, and future ideas can be more ably formulated.

International cooperation for such development and for dissemination of knowledge has come from numerous sources. As examples, it will be sufficient for me to quote only a few. The widespread medical journals, the interlibrary facilities, the large numbers of foundations devoted to medicine, such as Carnegie, the Rockefeller, the China Medical Board, and the Colonial Development and Welfare, and the mergence of specialized agencies devoted to health of the United Nations, such as the World Health Organization, the cooperative efforts engendered by the Colombo Plan countries and the South-Pacific Area Commission, the Inter-Univer-

sity Exchange Scheme have all furthered and encouraged international cooperation in postgraduate medical education.

My country has benefited enormously from international effort. We have profited by the postgraduate medical education given to our students in universities and other medical institutions in countries overseas, particularly the United Kingdom and Australia. We have profited even more by the experts from other countries coming to our areas and working among us. A group of American scholars working in the Institute for Medical Research in Kuala Lumpur discovered, quite by accident, but by design insofar as they were in Kuala Lumpur, that chloramphenicol is as much a specific for typhoid as it is for tropical typhus. Another discovery that might be profitably mentioned is the work of the Medical Research Council in Singapore when they studied conditions in the tropics in close liaison with the department of physiology. We have, of necessity, had to limit postgraduate training facilities for our doctors to countries we know of more intimately than others. Consequently, many of our scholars go to the United Kingdom or to Australia and a few to the United States of America and Canada for such postgraduate education.

It does not, however, follow that other countries cannot contribute to our knowledge. In fact, I believe that the more widely spread our ideas and purposes are, the more shall we profit by collision of ideas which might appear to be antagonistic, but which I do not believe are in fact antagonistic in medicine.

International cooperation, therefore, in the field of postgraduate medical education should yield far more practical results than the insularity of breeding and thought which would impose limitations to progress. It is by appreciation and realization of the significance of various facets which constitute what might be the truth that we may be enabled to get a glimpse of the ultimate truth.

Purpose of Medicine

If I may be permitted to digress a little, medicine is drifting away in recent years from its purpose. We have been so much engrossed with the significance of bacteria and viruses, of antibiotics and pharmaceutical preparations, of the heart and the lungs and the liver and the other viscera that we are in grave danger of not realizing that the human being is much more than the sum total of all his constituent parts. We are dealing with a being—quite apart from our religious teachings that there is a soul—we are dealing with a being which has a physique, which has intelligence, which has aptitudes, which has attainments, which has interests, and which has disposition, and this being has been subjected to numerous stresses and strains by the environmental circumstances of his living. We have to realize that he is a thinking thing, a feeling thing, an emotional thing that has been molded and shaped by his environment either to live sensibly and in rapture with his fellow beings or as a rebel within them.

The fact that the word "disease" has been so distorted in its original meaning emphasizes how far medicine has departed from its original purpose. It is right that we should remind ourselves what disease is. It is not tuberculosis, it is not typhoid, it is not cholera or any of those descriptions that appear in textbooks. It is in fact "dis-ease." Does it really matter to the man whether he has cancer or hypertension if he is not at "dis-ease," so long as he feels no ill, so long as he works efficiently, so long as he thinks well, so long as he is able to contribute abundantly to his country and live joyfully. Can we as physicians be exonerated from the indictment that we have often made the "cure" of such patients more grievous than the endurance thereof? The World Health Organization defined health in a more liberal way than I have done. It says "it is a state of physical, mental and social well-being and not just the absence of disease."

While we accept the fact that organic pathology is likely to produce disease, we must take cognizance of this—that many more things than organic pathology can cause dis-ease. Now this presupposes a wider (and a more liberal) knowledge than that provided by the ordinary medical education, whether undergraduate or postgraduate. It presupposes a knowledge of a kind which embraces within it the humanities, the religions, and a deep understanding and sympathy for the living man and a sincere respect for the human personality.

International cooperation, while it is much greater than it ever was before in postgraduate medical education, is not yet sufficient. And the tragedy of it all is that developments in other fields of science, for example, nuclear energy and conquest of space, are proceeding so fast that we appear to be lagging behind. Not only this, we would have to face the challenge of these developments and, if in the hour of need we fail, we shall not only be held to blame but to ridicule as well.

Do not for one moment think that remote countries, underdeveloped countries, or small countries will not be able to contribute anything significant to the development of postgraduate medical education. Underdeveloped countries and such countries as I live in can contribute much, but the fact of our contributing something to your knowledge and your even greater contribution to us would be as nothing compared to the synthesis that will emerge as a result of this cooperative effort. A broader vision, a wider field, and a more deliberate appreciation and consciousness of our purpose and aims will be furthered by such efforts and I make an appeal here and now that we should intensify international cooperation in postgraduate medical education with the least possible delay.

VALUE OF RESEARCH FOR THE GRADUATE AND POSTGRADUATE MEDICAL STUDENT

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There is no need to document the value of medical research as a major factor in the constantly improving well-being of mankind. It could be convincingly contended that our knowledge of health and our control of disease have progressed farther in the last 50 or 60 years than in all the preceding countless ages of man.

Furthermore, it is unnecessary to declare the value of participation in research for a medical student who anticipates a career of either full-time investigation or part-time clinical research supplementing the practice of medicine. The methods and tools of research and the nature and conduct of investigation must be learned early. A physician who has done no investigation by the time he has finished his postgraduate residency training is unlikely to make significant research contributions in his subsequent career.

It is self-evident that research must continue to increase our understanding of man in health and disease and also that experience and training in scientific investigation are essential at an early stage in the education of the physician who intends to continue to carry on research. This presentation is concerned rather with the value of participation in research as part of the experience of a medical student who may not again work in a research laboratory, who has no intention of conducting further clinical investigation, or who will never write another scientific paper. Some training in research can contribute enormously to the education of such a physician, engaged entirely in clinical responsibilities, as is necessarily the case with most physicians.

Evaluation of Research Reports

Past research experience by a physician who is now fully engaged in clinical practice sharpens his judgment and enhances his evaluation of the research of others. "Medicine, a life-long study" requires the physician to keep abreast by reading the journals and listening to scientific papers. Research necessitates a struggle with data collected, requires a sifting and sorting of experimental results, insists on a recognition of deficiencies in the supporting evidence, and compels the reaching of conservative conclusions warranted by the objective findings. Experience in research warns against the pitfalls of inadequate numbers of observations, faulty controls, inaccurate measurements, the intrusion of chance, and the inherent variability of biological material. Engagement in research enhances the physician's judgment of conclusions reached in medical papers he reads, sensitizes him to inadequacies of evidence, increases his wariness of exaggerated claims, and tempers his acceptance of enthusiastic predictions.

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Address to the First Plenary Session of the Second World Conference on Medical Education, Chicago, Aug. 31, 1959.

Difficulty of Discovery

Research has been called "a way of making nature talk." But nature guards her secrets with intense jealousy and is loath to speak. Research reveals the painful difficulty of discovery.

To the layman, who reads only the newspaper or popular magazine accounts of discovery, the pathway is easy. To the more sophisticated person, such as a medical student or a practicing physician, somewhat familiar with research literature, the difficulty of making a contribution to knowledge becomes more apparent. But it is only the student or physician who has actually participated in research himself who is completely aware of the tremendous effort and patient toil which are exacted of an investigator who establishes even a very little new fact or a causal relationship.

A celebrated exception to this axiom was the discovery of vagus material by Otto Loewi. He recounted that he had an idea one night, in bed, and went to his laboratory the next morning to test his thought. In this instance, only a day elapsed between the idea and the demonstration. New principles of broad physiologic application emerged: not only the concept of neurohumoralism but also eventually the theory of chemical transmission of nerve impulses across synapses.

Much more characteristic of the unhasty pace of research discovery is the story of insulin, with the long and labored span of three decades between the experimental production of diabetes in dogs and the beginning of its control in man. Years of frustration were the only rewards of investigators probing this most jealously guarded secret of nature. The dual function of the pancreas, as a digestive and an endocrine gland, the concept of hormonal secretion, the idea of replacement therapy, the enzymatic destruction of islet secretions in crude pancreatic extracts, the correct pH to preserve the islet-tissue hormone, the embryonic history of the pancreas (noted and utilized by Banting), the purification of the embryonic extracts of islet tissue free from digestive secretions,

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and, finally, the therapeutically successful injection of these extracts into diabetic dogs took years and years and years of labor and failure and frustration. The struggle for insulin soundly documents that hard lesson of research experience, the difficulty of discovery.

Pursuit of a Scientific Hobby

Even though a physician may do no research or engage in a limited specialty such as cardiology, a past research experience may provide a rewarding hobby or special interest to be followed at least in the literature and perhaps also at scientific meetings.

The postgraduate resident physician who spends only three to six months in a cardiac catheterization laboratory might be prompted to follow subsequent findings in this field with considerable gratification. He will observe with special appreciation the latest developments in artificial blood circulation, extracorporeal aeration of blood, refrigeration, control of cardiac arrest, electrical pacemakers, intracardiac prostheses, repair of valves and septal defects—the many discoveries to come in the control of congenital and acquired cardiac defects.

Alertness to the Unexpected

Research develops an alertness to the apparently inconsequential. In carrying out any research project, it soon becomes apparent that it is essential to be forever on the alert for an unexpected observation sometimes seeming almost to be an accidental occurrence.

Each such occasion must be given due weight. The incidental observations may prove to be far more important than the original goal sought in the experiment. The magnitude of Fleming's discovery was not at all apparent from his simple description of an experimental accident of vast moment: "While working with staphylococcus variants a number of culture-plates were set aside on the laboratory bench and examined from time to time. In the examinations these plates were necessarily exposed to the air and they became contaminated with various micro-organisms. It was noticed that around the large colony of the contaminating mold the staphylococcus colonies became transparent and were obviously undergoing . . . (destruction)."

This kind of alertness to apparently insignificant detail, not directly in the pathway of the moment's reflection or not immediately integrated into the experimental context, has yielded many a discovery. For lack of this sensitivity how many important discoveries were missed: the vector of transmission of the poliomyelitis virus, the arresting of mitosis in cancer cells, the dissolving of a blood clot in a coronary vessel.

Clinicians who rise above the common lot have, perhaps in many instances through research experience, similarly become allergic to the minute, the obscure, the incongruent. A few tiny petechiae may point to a subacute bacterial endocarditis in an obscure complex of signs and symptoms. A 30-year history of healed pulmonary tuberculosis might provide the diagnostic clue to a painful palpable mass in the pelvis.

Collaboration in Clinical Practice

Research provides lessons in teamwork. Little modern research of consequence is carried on by the lone investigator. More commonly in evidence is the combined effort of experts in several disciplines. Studies on poliomyelitis vaccine necessitate collaboration between bacteriologist, neurologist, internist, statistician, epidemiologist, biochemist, and pathologist and others as well.

Teamwork in clinical practice is equally necessary, particularly in dealing with complicated problems. In a modern clinic it is not unusual for experts from a half-dozen or more clinical specialties to collaborate in arriving at a diagnosis and determining management.

Who does not learn, perhaps in an experimental laboratory, this lesson of teamwork in the practice of medicine and the employment of consultations by a collaborating group will be much less than a good physician.

Persistent Routine

Research fosters a respect for persistent routine. Inspiration and glamour are not prominent in the continuing plodding which is demanded. The researcher patiently repeats the experiment again and again, week upon week, changing the procedure, perfecting the technique, analyzing the failures, month after month doggedly pursuing the goal with no assurance of reaching it. There is an abundance of routine and boredom demanding inordinate tenacity to continue the venture. What thousands of dull red blood cells counts for long hours of many months provided the evidence to Whipple that liver accelerates red blood cell production in anemic dogs! How many frog nerve-muscle preparations were carefully dissected by Helmholtz before he determined the speed of the nerve impulse!

Everyone who would contribute importantly to the world's work must learn this lesson of persistence in routine. The President of the United States must spend a lot of time writing his name. The concert pianist must practice alone for hours on end. The physician must percuss the heart borders of the hypertensive patient again and again. The medical student must laboriously repeat white blood cell counts of the patient with an infection.

The rewards of research, or of medical practice, demand countless inglorious hours of stubborn work as routine as might be found in the performance of many a less pretentious task than medicine.

Highway of Discovery

Research provides knowledge and familiarity with one of the highways of discovery. The study and reading essential in carrying out a research project, determining what has gone before in this area and what yet needs to be done, are as different from the more casual reading of such material as actually traveling a countryside is different from reading a highway map. The gratification of such an excursion is intensified by the ultimate arrival at the end of the charted road where exploration into the unknown occurs.

The discovery is usually very modest. Often it is a negative finding, the posting of a warning on a dead-end street. Yet it is a discovery, new knowledge, light into the darkness, a penetration beyond the frontier. Discovery, great or small, of what was never known before, is an adventure to be cherished, an experience likely to color a physician's entire outlook on his work. The physician who is imbued with the spirit of investigation, augmented by research experience, will be a little more persistent in his diagnostic searchings, in his therapeutic efforts, or in his self-evaluation.

Summary

Experience in research as a medical or graduate student may stimulate a continuation of some investigation throughout life. Even if the physician does no research after his formal education, his earlier experience in investigation will prove of tremendous value, because research sharpens the physician's judgments of the scientific pronouncements of others, it reveals the painful difficulty of discovery, and it stimulates the pursuit of a scientific hobby. Research promotes an awareness of unobtrusive "accidental" phenomena which may be of great importance, it provides lessons in teamwork, and it fosters a respect for persistent routine.

Research acquaints the investigator and physician with one of the highways of discovery leading into the unknown.

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VALUE OF PARTICIPATION IN RESEARCH IN CONTINUING EDUCATION OF PRACTICING DOCTOR

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Education is a continuing process which is dependent on active studying. Without the critical application of one's mind to the subject, learning proceeds slowly and imperfectly and judgment is apt to be fallacious. The best of all study results when one applies one's energies to the elucidation of problems to which the answer is not known. This is usually called research. It is a broad field in which people with different types of talent may work successfully.

There are many ways in which research may be pursued. In all it is essential to know the background of the field of investigation; in professional work this demands a sound knowledge of some aspects of one's field of practice and an awareness of the type of problems that may arise in it. It is always concerned with wondering, pondering, dreaming, and speculating about the subject. It always has to do with formulation of problems, sometimes in a broad philosophy, sometimes in a much narrower focus. The persistent endeavor to comprehend the background and the gropings to clarify the problem are all part of the search; and it is the searching that is important in education, not getting the answer. That some person may already have found the answer is not pertinent to the process of learning.

Medical people vary greatly in their essential interest in investigation. In some it is so keen that they are impelled to spend their lives either in experimental research or in the intensive investigations of disturbances of body and mind in health and disease. These persons usually stay in university centers and any practice undertaken is as an associated and minor interest. Others make their living in various fields of practice; it is with them that we are concerned in this discussion.

It is a great mistake, however, to think that the habit of inquiring and the genius for searching are limited to those who devote their lives to organized research. It is equally wrong to expect the busy practitioner to unearth many new facts or make

From the Department of Medicine, University of Toronto.
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striking advances. His searching is of a different intensity, spread at first over the broad area of his practice. Should he work in a university center, and especially if he restricts his practice to a special field, it is easier for him to focus his attention on a specific problem, and often to work in association with laboratory colleagues. In more general practice, the field is broader but many have a largeness of mind capable of embracing a wide field in an intelligent survey. They must at first look at a whole landscape, but the scrutiny may lead to observations that demand focal study, sometimes with the help of others.

Need for Study in Field of Work

The practicing doctor has many opportunities to engage in useful research work, but his accomplishments are likely to be restricted by lack of time to think about his problems and formulate them clearly. The more general his practice, the greater is this difficulty. It is of first importance, therefore, that he study in a field that he knows and that his projects be concerned with some aspect of his regular work. Just as teaching and research should not be separated, so practice and study should go hand in hand. Active studying stimulates the teacher, clarifies his ideas, and helps him gain a clearer vision of fundamental principles, making him a better teacher; in a similar way it stimulates the practitioner, sharpens his powers of observation, and throws light on his daily problems, making him a better doctor. Good habits of thinking, observing, planning, discriminating, and judging well are engendered and nurtured by persistent searching; these habits of investigation come to be used in all that one does. Their development requires constant application; hence they must arise and grow from daily use, the research becoming a concentrated effort in problems met with in ordinary work.

A research hobby outside one's regular work is seldom helpful in education. To devote all his spare time to an extrinsic subject, such, for instance, as the study of tissue culture, actually tends to reduce a practitioner's interest in his patients and their disorders. If he has great talent for more fundamental research, however, it may lead him from practice into full-time research in the field of his interest and aptitude. Banting taught physiology as a side interest when he began to do general practice after World War I; the idea of a search for insulin soon took possession of him and changed his life's work.

Continued Study of Patients—Basis of Research and Education

The pursuit of research in practice is not, and should not be, a separate component of a doctor's life. It is not like a coat that he puts on in moments of freedom from strain. It does not usually begin as a conscious effort in one field. It never comes with ease but only after long effort and disciplined thinking. Problems for study become apparent to those who put their hearts in their work and work for the joy of it, who pursue their profession with unrelenting diligence and with an inquiring mind willing to question established principles that do not satisfy the challenge of experience. These problems arise chiefly out of one's own experience and thought, although reading, discussion with one's associates, and the encouragement of talented colleagues may provide the initial stimulus and give continuous support to the work. "Clinical research ranges from the making of observations which are incidental to, and inseparable from, good practice, to systematic investigations undertaken deliberately and often over long periods with the object of answering specific questions. The former has always been an activity of good practitioners and, apart from seeing that it receives appropriate support, requires no special organization." [1] Its practice may, however, lead to the formulation of specific questions and the prosecution of more systematic research.

The question is often asked, "How should a practitioner begin his study?" It may be answered, to paraphrase Peabody's [2] famous remark about care of patients, by saying that the secret of the study of patients lies in studying one's patients. To further the study, however, there are certain practices to be followed and habits to be formed which, if persisted in, always have a good educational effect and commonly lead to useful advances in knowledge.

One has to do with the keeping of good records. The constant practice of describing symptoms, signs, and other important factors in concise, clear, and exact language enhances one's ability to recognize important findings and place them in proper perspective. It focuses one's attention on the more significant observations and provides the data for later examination and study.

Another is concerned with the habit of thinking and pondering over interesting findings, difficult problems, and striking phenomena. "Real thinking is an acquired skill founded on practice and habit, like playing a piano, and how well we can think at any given time will depend on how much of it we have already done. Nor can we think at random; we can only add one more idea to the body of something we have already thought about." [3] The process of thinking is facilitated by talking over our interests with competent, responsive colleagues and discussing our problems with them. The expression of our thoughts in conversation leads to clearer formulation of ideas in our own minds.

Such practices lead us to regard each difficult case as a problem which can be solved by data at hand or easily obtained, a practical research attitude which, if persisted in, will soon provide a rich background of knowledge. One begins to think and talk in terms of one's own experience, thus modify-

ing knowledge based on reading and on the teaching of others. When one begins to describe his own results his methods of study are developing well.

The careful preparation of reports in clear appropriate terms is a necessary part of the discipline of research. It opens one's conceptions to exacting scrutiny and shows up the shortcomings and imperfections of observations and impressions. The examination of data and formulation of opinions comprise a constructive effort from which ideas arise to prepare the ground for making significant new observations.

As thoughtful and intelligent doctors pursue their practices, interesting differences become apparent in them. They do not all see a given patient in the same light. Manifestations that interest one and call for, even demand, his study pass unnoticed or little regarded by colleagues of apparently equal understanding and experience. This wonderful quality of awareness soon distinguishes the man with genius for research. It is partly inherent, depending on powers of association, memory, imagination, sagacity, and insight, but it flourishes only in fields well cultivated by long periods of study. Discoveries ascribed to chance are usually, perhaps always, due to the possession of this happy faculty of recognizing important observations. Considering this phenomenon from a different point of view, Cardinal Newman [4] spoke of the ability to make an instinctive just estimate of things as they pass before us as a quality "which sometimes indeed is a natural gift, but commonly is not gained without much effort and the exercise of years." It is a faculty which was exhibited with dramatic effect by Fleming when he recognized as important the inhibited zone around the colony of penicillium in the staphylococcic culture plate. It has been demonstrated with less spectacular, but still gratifying, results by countless practitioners who have often gone on to pursue intensively the problems thus drawn to their attention.

Adverse Influences in Practice of Medicine

There are certain influences in the practice of medicine which have an adverse effect on the prosecution of research. Perhaps the most deleterious is being too busy to have time to think, too weary and preoccupied to read or wonder. Being always in a rush and hurry tends to quench the sparks of imagination and inspiration, inhibit the powers of association, and dull the memory. The care of patients then becomes more and more a matter of routine, leaving little opportunity for learning. Actually it is easy under the best of circumstances to slip into mechanical procedures, for, as Ritchie [5] has said, "it is a standing temptation of mankind to put routine, which calls for no thought and little effort, in place of judgment which calls for both." Development of judgment is essential for all good studying.

Almost as bad is to have a false conception of research: to think it can be done easily; that it is a matter of accumulating data from a series of tests and not, as it must be, an active discriminating process in one's own mind. What is done easily will neither answer important questions nor promote one's education. The failure to realize the need for hard disciplined thinking and constant scrutiny of one's observations and deductions is almost an insurmountable handicap. Those who fail to appreciate the difficulties in the way become easily discouraged like obese patients on low-calorie diets who expect early dividends in reduction of weight without commensurate effort and determination in sticking to the regimen.

Other retarding influences include the attempt to do so much that little can be accomplished because of failure to restrict the focus of one's studies; the deviation of one's efforts to make use of expensive equipment and recording devices in the belief that the use of these instruments is more scientific than the direct pursuit of one's problems by simple appropriate methods; and the desire for the glamor and prestige of research rather than for the interest, pleasure, and satisfaction of searching.

Special Vantage Ground of Practitioner

The practitioner has a special vantage ground for certain types of study. He can follow the natural course of disease and its modification by all manner of influences: a huge field of unending interest and challenge. He can study the efficacy and dangers of new remedies. Every effective measure opens new avenues for research into the fundamental nature of the disorder affected. Each great advance raises far more questions than it answers and opens doors for useful investigation to practitioners who can see the opportunities. Any clinical field in which there is nearly universal acceptance of current ideas is ripe for critical questioning and productive research.

The exact observations of Trousseau in the middle of the last century led him to doubt the value of blood-letting and other current measures used in treatment of people with strokes and he ceased to use these methods because, as he said, "experience has taught me that patients do better without them." William Pickles, during his years of general practice in Yorkshire, in addition to throwing much light on the epidemiology of common infections, was the first in England to report cases of Bornholm disease.[6] Many similar examples of important contributions by practitioners of former and modern times could be cited if time permitted.

The great contribution of practitioners as a body cannot be cited in individual instances. They play a large, if inconspicuous, role in the advancement of medical knowledge. The accumulated good sense of a large number of thoughtful doctors has a wonderful influence: it dampens the excessive swings of

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medical fashion; buffers the overly enthusiastic claims for ill-founded methods of diagnosis and treatment; acts as the ultimate jury in clinical trials; and has a firm, strong educational influence.

The general principles of research methods and study are the same, no matter what the field. But techniques used vary greatly and each must learn those appropriate to his problem. To produce much new knowledge requires virtually all the time of the investigator, allowing little opportunity for practice except in fields restricted to his special interests. But the critical research attitude of honest thinking and penetrating doubt on the part of the doctor in active practice is a catalyst which speeds up the learning process and gives new knowledge at a different but important level. It broadens his mind, increases his comprehension, and, by its inherent discipline, raises the standard of all aspects of his practice and of that of his closer associates.

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DANGER TO CHILDREN OF INFECTION FROM EXPOSURE TO URINE CONTAINING TUBERCLE BACILLI

RESULTS OF A STUDY MADE WITH THE MANTOUX TEST

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The possibility that children might acquire tuberculosis from parents with genitourinary tuberculosis was studied in 50 children under 13 years of age. All were progeny of 28 parents who were known to be discharging Mycobacterium tuberculosis in the urine although they were free from signs of open pulmonary tuberculosis. Eleven (22%) of the children gave positive tuberculin reactions, as compared with the accepted figure of 10% or less for the incidence of positive reactors in the general population of the same age. Since the tuberculin-positive children did not show evidence of tuberculous foci in the lungs or elsewhere, it was conjectured that the infection might be gastrointestinal. Consideration of prevailing habits in the disposition of laundry, the use of water closets, and the handling of food leads to important suggestions for hygiene in family living.

The question of whether "precautions against contagion" should be taken for patients with urine cultures positive for Mycobacterium tuberculosis has never been adequately studied, as far as we can determine. As a consequence, few hospitals take "precautions against contagion" when dealing with patients suspected or known to have live tubercle bacilli in their urine. At the same time, it is easy to demonstrate that urine has a wide distribution, even among relatively fastidious social groups. This at once becomes apparent when any member of a family is given medicaments containing a blue or red dye. First the color permeates the underclothing and bed sheets of the patient, later it will appear on the pillow cases, and still later it may appear on the dish towels and on the dishes in the dish cabinets. The walls and floor around the toilet will be stained for a surprising distance by bouncing droplets which had previously gone undetected because they had been colorless. The laundry hamper may become indelibly stained, if the medicament which colors the urine is administered for a long enough period. In less fastidious families the interface between the infected urine and the family members is expanded still further. When the urinary urgency, frequency, and some-

From the Research Unit for Genito-Urinary Tuberculosis, Columbia University College of Physicians and Surgeons, Presbyterian Hospital, and Kingsbridge Veterans Administration Hospital.

times involuntary voidings of patients whose bladders are irritated by tuberculous ulcers is added to the above conditions, the possibilities for exposure of other family members to the tuberculous urine become still greater.

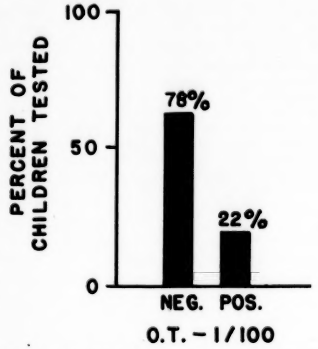

Fig. 1.—Results of tuberculin tests of 50 children exposed exclusively to parents' urine containing M. tuberculosis.

In an effort to document the fact that tuberculous urine might be infectious we undertook to do tuberculin tests on the available children of our patients with genitourinary tuberculosis. We selected those children exposed to tuberculosis for whom the urine was the only possible source of the organisms and excluded those who had possibly also been exposed to the tuberculous sputum of the few patients who had open pulmonary tuberculosis intercurrently with their urinary tuberculosis. This reduced the number of children who met the criteria of this study to a total of only 50. It must be remembered that male patients with genital tuberculosis tend to have an impairment of fertility to begin with, so that even this small number of children represents the results of five years of testing and case finding among a group of some 300 men and women who are currently under treatment with us for genitourinary tuberculosis.

Method

Children were accepted for the study only if they were exposed to the parent during the period when his urine was known to be positive for M. tuberculosis. If the father or any other contact of the child had open pulmonary tuberculosis at the same time, the child was excluded from the study. Children over 12 years of age were excluded arbitrarily. All children who were included were given an intradermal test, with use of old tuberculin (O. T.) (Mantoux test), in strengths ranging from 1:10,000 to 1:100. All children whose results were reported as negative were tested with 1:100 old tuberculin given intradermally. It was necessary for us to accept 14 children who were tested by other physicians, according to our specifications, because of factors which prevented their traveling to visit us.

Results

Fifty children were screened, accepted, and tested under the conditions of the study. These 50 children were the progeny of 28 parents, all of whom had been discharging M. tuberculosis in the urine at the time these children were exposed. This had been proved by the finding of positive urine cultures or by guinea pig inoculation tests made with the urine from the patient.

Of the 50 children 11 (22%) showed a positive reaction to the intradermal tuberculin test, while 39 (78%) showed a negative reaction (fig. 1). This incidence appears significantly higher than the incidence to be expected among children in the northeastern section of the United States, where this study was conducted. All of the children with positive results of the tuberculin tests then had chest and abdominal x-ray studies made, as well as urinalyses and physical examinations by their own pediatricians. In no case was any evidence of a primary lesion located.

It was interesting to observe that of 28 parents with urine positive for M. tuberculosis who brought their children to be tested all of the infecting was done by only 8 (29%) of the 28 parents with urinary tuberculosis (fig. 2). These eight parents had a total of 16 children, of whom 11 (69%) had a positive tuberculin reaction (fig. 3). This suggested that these eight parents exposed their children more thoroughly than the other parents, since they succeeded in infecting their children 69% of the time, whereas the other, larger group of parents did not infect any of their children. This suggests that the group of parents who infected their children so thoroughly did so because of some other factor, such as closer personal contact or less careful personal hygiene. It

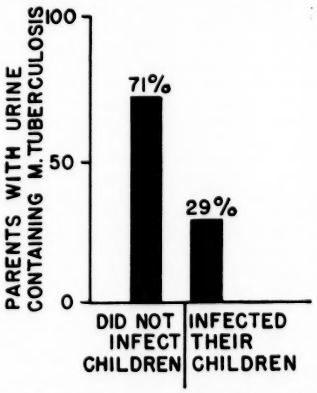

Fig. 2.—Percentage of parents infecting their children.

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is also possible that their bacteria were more virulent. A study of these factors is now being undertaken among these patients.

Comment.—The 22% of these children with positive tuberculin reactions after exposure to urine containing M. tuberculosis is significantly higher

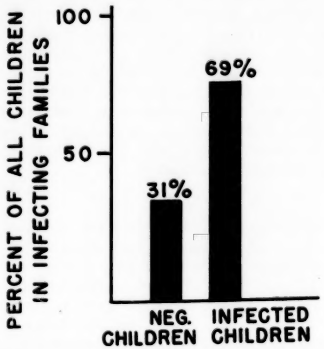

Fig. 3.—Percentage of children of infected parents showing positive and negative results of tuberculin test.

than the incidence of positive reactors among the general population of the same age. This has been reported as 10% or even lower by Braun (fig. 4).[1]

It must be realized that most of these patients did not know they had urinary tuberculosis at the time that they exposed their children. There is frequently a lag of many months between the onset of the first urinary symptoms and the diagnosis of urinary tuberculosis. During this time the child of a patient who is especially demonstrative toward his family will be thoroughly exposed while playing with the patient, crawling into bed with him, or playing in the soiled laundry hamper among his contaminated undergarments.

Since none of the children who showed a positive tuberculin reaction showed any evidence of pulmonary disease by x-ray examination, nor of other tuberculous foci by pediatric examination, it was conjectured that the infection might be in the gastrointestinal tract, probably due to the ingestion of tubercle bacilli from the infected urine of the patient. Whether the bacilli were picked up from spatterings on the bathroom floor, from the patient's bed linen, or from the soiled laundry hamper could not be determined. Certainly children are very susceptible to the disease, which may lie dormant for several years before flaring up at puberty or later in life. The chances of a flare-up in a child who has a positive tuberculin reaction early in life have been demonstrated to be much greater than those among children who have had no such early infection.

Precautions

It is our policy to put patients who are known to have M. tuberculosis in the urine on "precautions." If possible, children should be removed from the household, or the patient should be transferred to a hospital, at least until he is started on antituberculosis chemotherapy. While in the hospital the patient should be kept on strict dish and linen precautions. If it is necessary for the patient to be at home, the toilet area should be carefully watched, and the patient should make absolutely sure that all of the urine goes into the toilet bowl and that spattering is kept to a minimum. It would probably be advisable for male patients to void in a sitting rather than a standing position, to minimize splashing of the urine. The toilet bowl and the underside of the toilet seat should be swabbed with an antiseptic solution, such as dilute sodium hypochlorite solution (Clorox), after every voiding. The area around the toilet should be washed with a disinfectant soap solution daily, lest dried urine combine with dust particles and be inhaled by children playing on the bathroom floor. Mops or rags used to clean this floor could spread infection to other parts of the house, and should be used only for this particular bathroom.

Where possible the patient should have his own private bathtub and toilet. In cases where this is not possible the tub should be cleaned with a disinfectant after each use by the patient. Perhaps the patient could use the bathtub last, which would

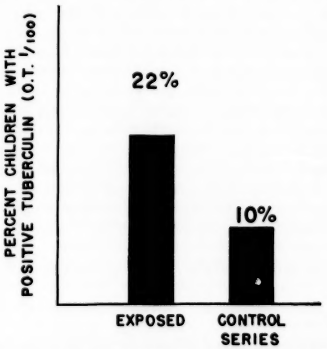

Fig. 4.—Percentage of positive reactors among children exposed and those not exposed (control series from Braun[1]) to urine containing tubercle bacilli.

enable the disinfectant to act for at least six hours, if permitted to dry on the tub. Bathroom doorknobs should be disinfected daily. The patient should take special precautions to wash his hands thoroughly with soap and water after leaving the toilet, but should be careful to turn the spigots by covering them with a paper towel before touching them. The patient should use paper towels, because they

can be burned. All other bath towels, clothing, underwear, and bed clothing of the patient should be stored and washed separately. The children should not be permitted to play on the patient's bed or in the laundry hamper where the soiled linen is placed.

The use of colored linen and towels for the contagious person is effective as a further control measure, even though it is resented by some patients. When the patient's bed is made, any unnecessary shaking or other movements of the sheets should be avoided. The windows should be opened and as much sunlight as possible introduced into the room. The bed linen should be changed as often as possible. Pillows and mattresses should be exposed to direct sunlight for at least six hours each week and the person who makes up the patient's bed should wear a mask to minimize the inhalation of tubercle bacilli. If a urinal or other vessel is used by the patient during the night, it should be washed in soap and water and boiled for 10 minutes each morning. Other furniture can be disinfected to some degree by exposure to direct sunlight for at least six hours.

A separate laundry bag should be used for the patient, preferably a disposable paper bag which can be burned. Contaminated clothing should be washed separately and soaked in a germicide for a sufficient time, or boiled for five minutes. The possible use of heavy metal salts to impregnate clothing and bed linen and thus render it permanently sterile is now under investigation.

In the past several cold sterilizing agents for M. tuberculosis have been tested by this research unit, in an effort to determine the best method for sterilizing cystoscopes. It was found that immersion of the instruments for one hour in the commonly used disinfecting solutions containing quaternary ammonium compounds, phenolic agents, and even formalin vapors after immersion did not kill all tubercle bacilli. The use of 10% formalin solution was uniformly effective in killing all tubercle bacilli after five minutes. This agent is not practical for household use. Boiling or autoclaving for 10 minutes was found to be completely effective. Immersion in strong solutions of chlorine-type disinfectants and detergents was not completely satisfactory at the end of one hour but may be satisfactory at the end of two hours.

Children exposed to patients with active tuberculous infections of the urinary tract should have an intradermal tuberculin test up to the strength of 1:100 approximately every six months, if the maximum precautions are to be taken. The Vollmer patch test is only acceptable if the result is positive. If it is negative, the child must be retested with an intradermal test up to the strength of 1:100, with use of old tuberculin. If the tuberculin test is positive the child should certainly have a chest x-ray, sedimentation rate determination, urine examination, and general physical examination in an effort to locate the focus. Calcified mesenteric lymph nodes may not appear for some months or years after a tuberculous infection of the gastrointestinal tract. Recent studies by the United States Public Health Service have indicated that children with positive results of a tuberculin test who are given isoniazid have a lesser incidence of tuberculous infection later in life than children who have positive results of tuberculin tests and do not receive treatment.[2] With this background, perhaps any child with a positive result of a tuberculin test should immediately be started on treatment with antituberculosis agents, including isoniazid, under the direction of his pediatrician. Any suspicious symptoms such as loss of appetite, loss of weight, chronic cough, or fever of unknown origin should be immediately investigated.

Comment

We recognize that the number of children used for this study is small. Nevertheless, it has been difficult to collect even this small number of cases, over the past five years, and it constitutes the only bit of information on this particular subject which we have been able to uncover. Furthermore, it is recognized that patients with genitourinary tuberculosis have rarely been placed on urinary precautions in the past and that no evidence of contagion has been registered down through the years. On the other hand, such contagion would be difficult to detect, since the tuberculous infection would probably be in the gastrointestinal tract and might not make trouble until many years after the child had been exposed to urine containing tubercle bacilli. Thus the association would be difficult to trace.

We have seen one case of infection of a wife by the tuberculous semen of the husband. This complication is rare, having been reported only seven or eight times in the accumulated world literature, but, here again, there may be many more cases than is realized.

It is our practice to consider the patient to have noninfectious urine after the first five days of adequate antituberculosis chemotherapy. It is recognized that patients occasionally spill infectious urine even during treatment, but this is relatively rare.

Summary

We attempted to determine whether patients with live pathogenic Mycobacterium tuberculosis in their urine infected children who were exposed to this urine. Children were accepted for this study only if exposure to this urine was the only known source of the disease. Intradermal tests with old tuberculin, in a dilution of 1:100 (Mantoux test), were used in all instances.

Fifty children of 28 parents with urine positive for tubercle bacilli were tested with tuberculin. Of these 11 children (22%) gave a positive reaction to tuberculin tests. These children were traced back to 8 patients among the 28 who brought their children to be tested. These eight patients had a total

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of 16 children, of whom 11 (69%) were the positive reactors. This suggested that these unsuspecting patients had either closer or more intimate contact with their children or poorer personal hygiene.

Infection from urine containing tubercle bacilli can occur. This can be minimized by the proper disposal of urine from the tuberculous patient and the observance of rules of strict hygiene.

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PATHOLOGICAL REPORTS FOR MORTALITY STATISTICS

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It has been supposed that the accuracy of mortality statistics could be improved by requiring that statements of the cause of death, as originally reported on the death certificate, be subsequently revised in the light of the autopsy report. This hypothesis was tested in a study of 5,217 autopsy reports in the year 1956. Of this number only 794 (15.2%) indicated changes in the stated cause of death. The impact on the final statistics was practically negligible, and the gain in accuracy did not seem sufficient to justify the labor expended in making the proposed changes. Improvements in procedure are still possible, especially in some localities. Physicians should be encouraged to review gross autopsy findings before completing death certificates, but the proposed requirement that the pathologist submit a later report has evident disadvantages.

A communication to THE JOURNAL [1] suggested that mortality statistics would be improved if pathologists reported the results of autopsies to the vital statistics office in order that the cause of death as originally reported on the death certificate could be revised accordingly. Such a requirement has been in existence in New York City since 1945. During the period that the requirement was in effect changes in the assignment of deaths to particular causes, as indicated by autopsy reports filed subsequent to the death certificates, were routinely made. However, the specific effect of these changes on final statistical tabulations was studied only recently. Before the study was made it was deemed wise to evaluate the whole procedure and, particularly, to determine the extent to which pathologists actually reported autopsy findings.

Statements on the 1955 death certificates indicated that autopsies were performed in 10,599, or about 13%, of the 81,612 deaths in that year. When deaths certified by the medical examiner and deaths at home were excluded the proportion approached 23% of hospital deaths uncertified by the medical examiner. But autopsy reports filed numbered only 2,796, 26.4% of the 10,599 deaths in which an autopsy was reported on the death certificate. Review of the data revealed that no reports at all had been received from some hospitals, while reports from others varied from 10% of to several times the number of autopsies claimed on the death certificates originating in those hospitals. Thus it was obvious that autopsies were performed more often than appeared from the death certificates but that subsequent autopsy reports were filed for a relatively small proportion.

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Efforts to Improve Reporting of Autopsy Findings

As a result of these observations it appeared advisable that an effort be made to encourage submission of autopsy reports from those hospitals that had been deficient, in order that maximum benefit be obtained and to reduce any possible bias in the study planned. Accordingly, Commissioner of Health Leona Baumgartner communicated the facts about each hospital to its superintendent, with a request for compliance in the interest of improved mortality statistics. In their responses some hospital superintendents and pathologists entered objections

because of the considerable supplementary paper work required. In addition, however, two major points that are pertinent to this discussion were made: 1. The cause of death as originally recorded was said by some to be based customarily on gross autopsy findings, in any case in which autopsy was done. 2. Final autopsy reports, including microscopic findings, would not become available in many cases until long after the mortality statistics for any year had been tabulated. It therefore became even more important to determine whether further attempts to overcome obviously justifiable resistance were warranted.

As a result of the commissioner's request to the hospitals the number of autopsy reports filed in 1956 was nearly double that in 1955. The present report is based on the 5,217 reports for the later year. Of this total only 794 (15.2%) indicated changes in the causes of death. In many of these instances the change was of a relatively minor nature, i. e., within the same cause category or group of causes.

Causes of Death with Twenty or More Changes Resulting from Autopsy Reports in 1956 in New York City

Cause of Death*	Total Originally Recorded	Removed	Added	Net Deaths	Net Percentage Change
Pulmonary tuberculosis (001-008)	934	30	12	916	−2.0
Malignant neoplasms (140-205)	16,824	186	258	16,896	+0.4
Vascular lesions of the central nervous system (330-334)	5,598	38	11	5,571	−0.5
Chronic rheumatic heart disease (410-416)	1,392	36	59	1,415	+1.6
Arteriosclerotic heart disease (420-422)	30,634	171	115	30,578	−0.2
Hypertension with heart disease (440-443)	3,735	28	16	3,723	−0.3
Pneumonia (480-493)	2,689	44	44	2,689	0.0
Ulcer of stomach or duodenum (540-541)	729	6	22	745	+2.1
Cirrhosis of liver (581)	1,635	26	20	1,629	−0.4
Congenital malformations (750-759)	905	8	26	923	+2.0
Birth injury, asphyxia, atelectasis (760-762)	1,082	24	51	1,109	+2.4
Infections of newborn (763-768)	192	1	22	213	+9.9
Other diseases of early infancy (769-776)	1,408	68	8	1,348	−4.5

* Numbers in parentheses refer to rubrics of the International List of Causes of Death.[2]

Effect of Autopsy Reports on Statistics

The table lists those cause groups in which 20 or more changes were made as a result of the autopsy reports. Both numerically and proportionately the results are small. Except among causes specific for infants the maximum net change is 2.1%. In view of the total number of deaths involved for each category listed the relatively few reassignments appear unlikely to affect distributions by age, sex, or color to a significant degree, any more than they do the totals.

What effects do the changes in a specific category have on other causes of death? Where are those statistics removed from one category then assigned? Whence do those added to a given cause come? The two groups of causes of death with the largest numeric changes (arteriosclerotic heart disease and malignant neoplasms) should most frequently feature withdrawals from or contributions to other disease categories. Hence it will be illuminating to look more closely at these two groups.

Arteriosclerotic and Degenerative Heart Disease.—The term "arteriosclerotic and degenerative heart disease" as used in this paper includes rubrics 420-422 of the International List of Causes of Death.[2] These rubrics cover arteriosclerotic heart disease, including coronary artery disease, nonrheumatic chronic endocarditis, and other diseases of myocardial degeneration. Of the total changes in this group 53 represent transfers from one section of the group to another and thus show up both as 53 additions to and 53 removals from the group. Many of these constituted a transfer from coronary artery disease (420.1) to arteriosclerotic heart disease (420.0), because the autopsy report indicated the arteriosclerotic nature of the coronary artery manifestation; and in such instances the classification system requires their assignment to 420.0. These 53 cases represent 31% of the 171 "removals" from this category and 46% of the 115 "additions" to it. Thus in reality there were only 118 removals from and 62 additions to the group.

Of the net 118 removals 35 were reclassified as due to malignant neoplasms, 17 to chronic rheumatic heart disease, and 16 to pneumonia, while 50 were reclassified as due to a variety of conditions, no more than 5 under any other specific category.

Of the net 62 deaths that were reclassified in the arteriosclerotic and degenerative heart disease group 11 had been originally classified as due to vascular lesions of the central nervous system, 11 to pneumonia, 10 to hypertension with heart disease, 6 to malignant neoplasms, and 24 to a variety of other conditions, none of which exceeded 4 in number. The final total of deaths from this cause was found to be 30,578; the net change, from the prior total of 30,634, was −56 (0.2%).

Some of these effects on other causes were, it appears, partly compensating. Reclassification of the deaths originally or eventually supposed due to arteriosclerotic heart disease resulted in a net increase of 29 in deaths ascribed to malignant neoplasm (35 from arteriosclerotic heart disease to neoplasms and 6 in the reverse direction) and of 5 ascribed to pneumonia (16 from arteriosclerotic heart disease and 11 in the reverse direction). Even for those conditions where such compensations did not occur the numbers are relatively small. There were 17 additions to chronic rheumatic heart disease, little more than 1% of the total deaths ascribed to that cause. Eleven of the cases had originally been classified as vascular lesions of the central nervous system, about 0.2% of the deaths ascribed to this condition. The 10 deaths subtracted from the category "hypertension with heart disease" is a relatively minute proportion of the 3,723 deaths finally ascribed to this cause.

Malignant Neoplasms.—As for the changes recorded for mortality from malignant neoplasms 152—81.7% of the 186 reclassifications from and 58.9% of the 258 reclassifications to this condition —represent but a redistribution within the category itself. Of the 34 net removals 6 were classified as due to arteriosclerotic heart disease, 6 to ulcers of the stomach and duodenum, and 22 to a variety of other conditions. Of the 106 net additions to the category of malignant neoplasm 35 had originally been classified as due to arteriosclerotic heart disease, 11 to cirrhosis of the liver, 11 to pulmonary tuberculosis, 10 to pneumonia, 6 to vascular lesions of the nervous system, and 6 to miscellaneous genitourinary conditions, while 27 had been originally classified as due to a variety of other categories. The final total of 16,896 deaths from this cause represented a net change of +72 (0.4%) from the previous total of 16,824.

As an example of the intragroup shuffling that occurs it may be worthwhile to look at the 152 deaths originally classified as due to malignant neoplasms, but for which changes in site only resulted from the autopsy findings. Of the total 152 in 90 there was merely a change of the cause from disease of one site to that of another within the same anatomic area; for the remaining 62 the site of the primary lesion was determined as belonging to a different anatomic system.

Of the 90 deaths from cancer shifted within the same anatomic system 33 were reassigned from one organ in the digestive tract to another. The pancreas, with 19 cases, was most frequently involved in these changes. The gross changes were +10 (1 reclassified from the stomach, 1 from the large intestine, 7 from the biliary passages, and 1 from the liver, unspecified as to whether primary or secondary) and −9 (3 reclassified to the stomach, 1 to the large intestine, 3 to the biliary passages, 1 to the liver, and 1 to the peritoneum and mesentery), a net change of only one death. The biliary passages were involved in 12 changes, the large intestine in 11, the liver in 8, the stomach in 6, and the rectosigmoid in 4. Five other sites were involved in a total of six changes.

As a result of these shifts in classification of fatal neoplasms within the digestive system the number of deaths assigned to disease of the biliary passages increased by six, those to disease of the large intestine by five, of the rectosigmoid by two, and of the primary liver by one. Reclassification decreased the deaths assigned to disease of the liver (unspecified as to whether primary or secondary) by six, to disease of the stomach by four, and by one each the number of deaths classified as due to disease of the duodenum, pancreas, peritoneum and mesentery, and abdominal viscera.

Obviously, none of these transfers is numerically significant, in view of the total number of deaths from cancer assigned to these sites. This additional accuracy does not contribute enough to improvement of the resulting statistics to warrant the labor expended in making the changes.

Comment

The clinical determination of the cause of death may usually be inferred to be wrong if it is not confirmed at autopsy. Autopsy findings in the individual case are highly important to medical science and research.[3] The usual studies of this type have been limited to analyses of the autopsy reports only,[4] thus introducing bias due to selection of the study group,[5] giving an exaggerated impression of errors in community mortality statistics,[6] and clouding the usefulness of mass mortality statistics as leads for careful clinical investigation.[7] Actually, when individual errors are combined in community mortality statistics, it is found that they cancel each other out to a great extent. Even though final figures for any specific cause are actually changed, the modification is so small that rates computed are not likely to be affected, except in infant mortality where substantial reclassifications of cause of death result from autopsies.

These findings from the New York City experience led to the conclusion that, in the city at least, changes in mortality statistics resulting from submission of subsequent autopsy reports do not in general warrant the additional work required on the part of the pathologists and the nosologists. Consequently, the board of health has decided to amend the Sanitary Code to limit the requirement for autopsy reports to deaths in infants.

Despite the fact that attempts to encourage complete reporting of autopsy findings resulted in doubling the number of reports, such reports obviously represented no more than half the number of autopsies performed. This paper has assumed that those autopsy reports submitted were an unbiased sample of all autopsy results, i. e., that no different results would have been found if reports of all autopsies had been available. This opinion is based on the observation that results of autopsy corrections in 1956 were no different from those in 1955, although only about half as many reports were received as in the later year.

One other factor should be emphasized. The causes of death as originally reported on the New York City death certificates have been said to be based often on gross autopsy findings. As a matter of fact the manual of procedures used in the hospitals states, "It is important to emphasize here that the death certificate must be filled out as soon as the autopsy has been completed and the cause of death has been certified by the pathologist." [8] Unquestionably, the effect of subsequent autopsy reports would be reduced to the extent that the gross findings are already reflected in the original report. Moreover about 68% of deaths in New York City occur in hospitals where a complete examination or an indicated surgical intervention may have been helpful in verifying the diagnosis. If these condi-

tions should differ in other areas, reports of autopsy findings might produce more substantial changes in mortality statistics.

However, the data reported in this paper give clear indication that in New York City reports of autopsy findings have not changed mortality statistics to the extent that might have been anticipated. If frequent reliance on gross findings of autopsy examinations for cause of death on the original death report accounts even in part for the relatively minor changes in mortality statistics derived from autopsy reports, then review of the gross findings by the signatory physician before completing the death certificate should be uniformly encouraged. Such a procedure may produce more tangible results in a simpler fashion than a requirement that the pathologist submit a later report.

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EVALUATION OF AN OXYGEN THERAPY UNIT

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A portable tank with a capacity of 56 liters of compressed oxygen is equipped with control valves, pressure gauge, plastic bag, and mask for use in short-period oxygen therapy. A unit of this sort was tested on six subjects under conditions permitting continuous determinations of oxygen concentration in the air of the oropharyngeal passage and of oxygen saturation in the blood of the ear. In addition, blood samples were obtained for determinations of arterial oxygen and carbon dioxide concentration in four subjects asleep under thiopental. The flow from the tank was initially about 6 liters per minute and declined as the pressure fell. It gave satisfactory oxygen and carbon dioxide values in unconscious persons for about 12 minutes. When the rate of flow declined below 4 liters per minute the elimination of carbon dioxide from under the mask was inadequate, so that after the 12th minute there was a significant degree of hypercarbia.

Many companies have long offered various-sized small tanks containing oxygen for resuscitative purposes. The armed forces, notably the Air Force, have employed such tanks to augment oxygenation, possibly of pilots and allied personnel during bailouts. There has developed lately a concerted effort to sell these oxygen units to the lay public. Numerous claims have been made for their efficacy in cardiovascular, respiratory, and possibly central nervous system emergencies. One of these units (fig. 1) has been made available to us for evaluation of its usefulness and effectiveness under conditions simulating the acute circumstances wherein such apparatus may be employed.

Physical Attributes

This unit consists of a small green tank containing oxygen and has a gauge which indicates the amount of pressure exerted by the oxygen within the tank—in this instance, 1,800 lb. per square inch (122 atmospheres). Narrow-bore rubber tubing leads from an orifice of this tank and conveys the oxygen to a small plastic bag and mask. A small piece of elastic band attached to the mask secures it to the face of the user. The tank has a capacity of 56 liters

From the Division of Anesthesiology, University of Illinois, College of Medicine.

of oxygen. Reports from the manufacturing company state that the tank, itself, is capable of withstanding pressures of at least 4,000 lb. per square inch (272 atmospheres), so that from the standpoint of rupture from internal pressure, it is fairly safe. The weakest point of any gas tank, however, is the juncture between the control valve, which serves as an egress or ingress for the gas, and the body of the

Fig. 1.—Single-unit oxygen therapy apparatus. Twin unit is also available.

tank. This unit is so constructed that the flow rate is limited or modified by a recessed flow control located in the cylinder itself. Such a safety feature prevents sudden discharge of the compressed gas.

Flow Valve.—The flow valve, which controls the flow of oxygen from the tank, may be opened with ease. This may be advantageous to a weakened person who is suffering from any acute condition necessitating oxygen. The orifice of the valve is designed to permit a certain rate of flow, so that expenditure of gas is spread over a longer period of time without necessarily limiting its effectiveness.

Pressure Gauge Indicator.—The unit has a gauge which shows the amount of pressure exerted by the gas inside the tank. An indicated pressure of 1,800 lb. per square inch showed the tank to be filled to capacity, i. e., 56 liters. When the flow valve was opened, a needle indicator on the gauge which normally pointed to the 1,800-lb. mark when the tank was full was observed to shift slowly to "empty" as the gas was discharged.

Refilling Tanks.—In view of the limited capacity of this tank, it was obvious that a need might arise to change tanks or to refill a tank if the contents were exhausted. A portable accessory that enables the user to refill the tank from a bigger oxygen tank accompanies the unit. Although this is a convenience, there are some dangers with such transfilling. The transfer of pressure from a big tank containing compressed oxygen at 2,500 lb. per square inch (170 atmospheres) to a small tank may cause explosions or fires, particularly in the presence of grease, lint, or oil at the orifice. It was noted also that, as the smaller tank is transfilled with oxygen under high pressure, heat develops due to the energy changes caused by sudden expansion and recompression of gas from the bigger tank. Although this may appear alarming, it is relatively safe.

Calculated Flow.—The flow rates described by the manufacturer, which were determined with a rotameter, were found consistent with our own measurements. We utilized a pneumotachograph calibrated against a precision Fisher-Porter flowmeter (fig. 2 and 3). The question that arose when we observed the decline in flow rate from the tanks tested was whether the unit gave equally effective oxygenation at the lowest point of flow as at the initial highest point of flow. The following tests were made to answer this question.

Tests on Volunteers and Patients

Oropharyngeal Area Oxygen Concentration.—Six subjects were used in this test, four normal persons and two patients who had just recovered from anesthesia. A Beckman oxygen analyzer was utilized to follow the oxygen concentration in the oropharyngeal area. A no. 16 oxygen catheter was inserted through one nostril into the oropharynx and connected to the Beckman oxygen analyzer. The

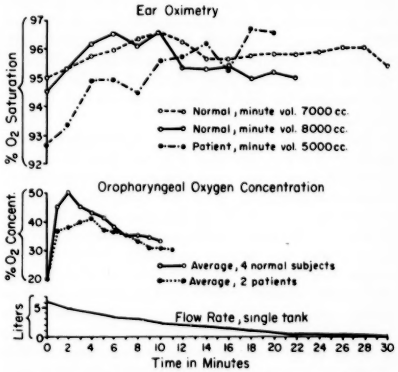

Fig. 2.—Ear oximetry findings and oropharyngeal oxygen concentrations.

face mask of the oxygenator unit was then placed loosely on the face of the recumbent subject and the oxygen allowed to flow. Oxygen concentrations were determined at regular intervals (fig. 2). In the normal subjects, the peak of oxygen concentration in the oropharynx was rapidly reached in the first two minutes and it then very gradually declined. However, at the 10th minute it was still at least

one and one-half times the concentration of oxygen in ordinary air. In the patients, the peak was reached a little later, i. e., in the third and fourth minutes; the concentration gradually diminished, but again, at about the 11th minute, it was still one and one-half times that in ordinary air. The difference was in the ability of the subjects to achieve peak concentration.

Oximetry.—The picture of oxygen concentration in the oropharyngeal area does not really reflect the uptake of oxygen by the blood stream in the alveolar area. Ear oximetry was therefore employed to determine the relationship between these. Three subjects were studied for this purpose, two who were considered normal and the third who had just recovered from anesthesia, who was completely conscious and cooperative. In one of the normal subjects the initial oxygen saturation was 94.5%; in the other it was 95%. In both of them the highest concentration was reached at a period of between 6 and 10 minutes, and both showed a maximum saturation of 96.5%. From this high point, the blood saturation gradually declined, until at about 21 minutes it was almost back to the original blood saturation at room air in one subject. In the other subject the higher oxygen saturation seemed to persist to about the 30th minute. The minute volumes of both subjects varied between 7,000 and 8,000 cc. per minute. The change in the third subject (the patient who had just recovered from anesthesia and had a minute volume of 5,000 cc.) was more outstanding. The blood saturation at the start was about 92%; it gradually rose to a peak of about 96% and was maintained at this level from the 14th to the 25th minute, at which point the administration of oxygen was stopped, since it was felt that the purpose for which the test was being carried out had been achieved.

One fact became immediately outstanding in this method of study, and that was the well-known observation that if the hemoglobin is quite well saturated with oxygen its ability to capture more oxygen even from an enriched oxygen atmosphere is almost minimal.[1] Therefore, in the normal subjects, whose hemoglobin was almost maximally saturated, one might conclude that any extra oxygen absorbed by the blood stream might have been dissolved in plasma and probably only a minimal amount taken up by the hemoglobin in addition, thus presenting a lower peak of oxygenation as compared to that of the sick person. On the other hand, the sick subject started out with a lower blood oxygen concentration and thus seemed to be more effectively oxygenated, probably because his hemoglobin was not as well saturated as the normal subject's and therefore its capacity to absorb oxygen was relatively greater. The other point, of course, is that his minute volume was obviously much smaller than that of the two normal subjects and thus his uptake of oxygen was much slower, as can be shown by the fact that the peak was reached at about the 10th minute. He also maintained a relatively higher peak much longer than the normal subjects.

Arterial Oxygen and Carbon Dioxide Concentration.—The final test was to determine actual oxygen concentrations in the arterial blood under conditions simulating those under which this unit might be employed. For this purpose, four patients were put to sleep with a 0.5% concentration of thiopental (Pentothal) sodium given by intravenous drip and were maintained in this sleep state for the period of time that the oxygen was administered from the unit. An arterial needle was inserted into a femoral artery and blood samples were obtained before oxygenation and at regular intervals thereafter. Arterial oxygen and carbon dioxide saturation were determined by both Scholander and Van Slyke methods. The values coincided closely. The results are shown in figure 3.

Just before the 15th minute, the anesthesia plane became light in patients A and B. They struggled and developed tachypnea, as shown by the low carbon dioxide tension and the rise in oxygen saturation. Respiration in patient A was subsequently overdepressed with thiopental and his minute volume dropped, followed by a fall in oxygen saturation. Proper anesthesia plane was eventually maintained without excessively depressing his minute volume, so that oxygen saturation gradually rose and carbon dioxide tension dropped. Patient B was maintained in a quiet plane of anesthesia. His respiration was depressed to some extent, as shown by the high carbon dioxide tension indicative of insufficient ventilation. The low oxygen tension at room air for patients C and D is due to the marked respiratory depression caused by rapid administration of thiopental initially. This was done in an attempt to achieve a steady sleep state with a stable blood level of thiopental that could be maintained by giving small increments intravenously.

A single tank and a twin tank were used, both of which gave an initial flow of about 6 liters per minute. The twin tank had twice the oxygen capacity of the single tank, i. e., 112 liters of oxygen as compared to 56 liters. The results were rather interesting. The arterial blood showed a gradual increase in oxygen concentration which began to be noticeable at about the fifth minute. This was also observed in four other subjects whose determinations were not included in the tabulations because of technical difficulties and errors encountered in the analyses of the blood samples, so that an incomplete series was obtained. The increase in arterial oxygen saturation continued up to the 10th and 12th minutes when the single tank was used and up to about the 15th minute for the twin tank. After the 15th minute, although there seemed to be an apparent persistence of a high arterial oxygen

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saturation, there was a definite tendency for arterial carbon dioxide tension to increase. This observation was disturbing, as herein may lie the danger to the unconscious person.

Comment

The determinations of arterial oxygen and carbon dioxide concentrations were considered the most critical ones in this study. A careful review of the results (fig. 3) showed the oxygen therapy units to have efficient value for the unconscious person in the initial 12 minutes for the single tank and for 15 minutes for the twin tank; this was indicated by increasing arterial oxygen concentration from preadministration levels and by maintenance of arterial pCO_2 within normal limits. These facts correlated quite well with the observations on oropharyngeal oxygen concentration and ear oximetry. The twin tank seemed to be slightly more effective than the single unit in this respect. After the 15th minute, although there seemed to be an apparent increase in arterial oxygen saturation, there was a concomitant rise in carbon dioxide tension. Oxygen flow from the tanks at this period was below the 4-liter-per-minute mark. The logical deduction from these observations was that, where oxygen flow fell below the 4-liter mark, the elimination of carbon dioxide from beneath the loosely fitting face mask diminished greatly, causing rebreathing of carbon dioxide from the increased mechanical "dead space."

To test this deduction, the following experiment was conducted. Carbon dioxide levels were determined under the mask applied to the face of a recumbent, conscious subject. A Liston-Becker infrared carbon dioxide analyzer was used to follow continuously and instantly carbon dioxide concentrations under the mask when no oxygen was flowing from the tank and when oxygen was flowing from the tank. With no oxygen flowing into the mask, carbon dioxide concentrations ranged from a normal of 5 vol. % at end of expiration to 6 vol. % within one minute. That carbon dioxide accumulated under the mask was shown by failure of the

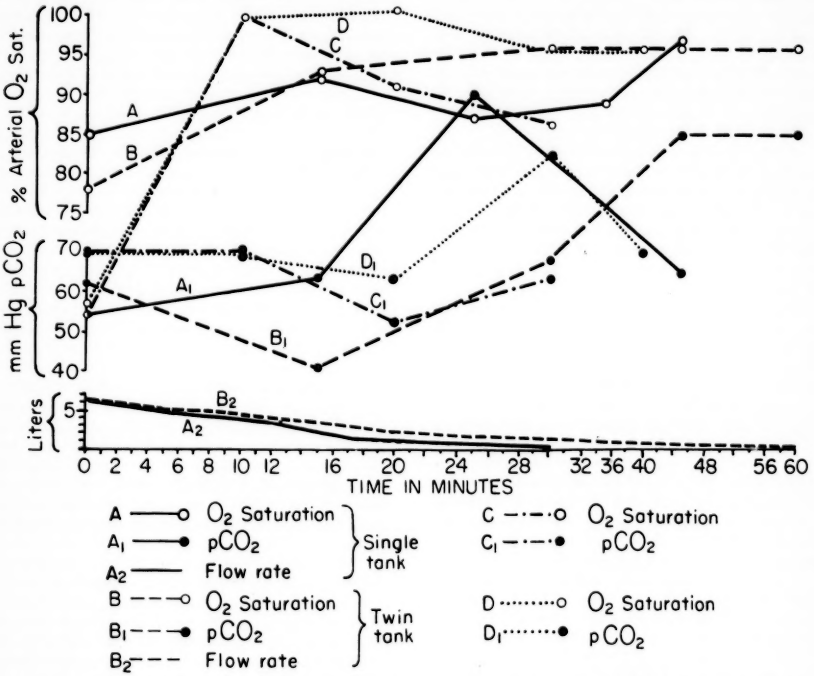

Fig. 3.—Analysis of arterial oxygen and carbon dioxide saturation in four patients under anesthesia with 5% thiopental.

carbon dioxide concentration to come down to zero during the inspiratory phase (staying at about 1 to 1.5 vol. %) and by hyperpnea in the subject. An oxygen flow of 6 liters per minute into the mask promptly reduced carbon dioxide concentration to 4 vol. % during the expiratory phase and 0 vol. % during inspiration. The favorable intramask concentration of carbon dioxide was maintained as long as the flow of oxygen remained at or above 4 liters per minute. A specially prepared tank which delivered a flow of 3.9 liters per minute was next attached to the mask instead of the 6-liter-per-minute tank. With this, carbon dioxide concentration was observed to rise to 6 vol. % during expiration and to 1 to 1.5 vol. % during inspiration within a period of one minute. Four liters seemed to be the critical limit below which oxygen flow from the tank became inefficient in helping to eliminate carbon dioxide from under the mask.

A definite pattern may be discerned from close scrutiny of figure 3. Arterial oxygen saturation gradually increased from preoxygenation levels during this period. Oxygen flow declined from an initial 6 liters for both types of tanks to 4 liters at the 10th minute for the single tank and at about the 12th minute for the twin tank. Carbon dioxide remained at preoxygenation levels during this period.

Hypercarbia, especially in the unconscious person, is definitely unphysiological. An earlier study by Reed and others [2] has shown that under certain conditions an excess of carbon dioxide accumulates steadily over a period of 30 minutes, after which time the results of hypercarbia become increasingly manifest and contribute greatly to the deterioration of the patient. Although hypercarbia might have been beneficial momentarily by provoking the "Bohr effect" (i. e., increased pCO_2 influenced the desaturation curve to shift to the right and thus provided for easier unloading of oxygen to the tissues), carbon dioxide became toxic when it was in excess of the normal concentration.[3]

It was obvious that in the apneic patient this unit was virtually ineffective unless some form of manual artificial respiration or mouth-to-mask ventilation was also employed.

Conclusions

From a practical point of view, both single and twin units did have the ability to augment blood oxygen saturation for a limited period of time. The greatest value lay in the first 12 minutes for the single unit and the first 15 minutes for the twin unit. During this time they were definitely capable of increasing arterial oxygenation and also aided in the efficient elimination of carbon dioxide. Doubling the capacity of the unit did not increase greatly the periods of effective oxygenation and efficient elimination of carbon dioxide.

Judging from their limited period of effectiveness, these units could be very useful in the initial 12 to 15 minutes of the acute phase of emergencies involving respiratory efficiency directly or indirectly. One assumes that during this period means for treating the patient on a more permanent basis would be arranged. Thinking on resuscitation has frequently been categorized into neat compartments, containing respiration in one, the cardiovascular system in another, and the central nervous system in another. Such thinking, though unintentional, is fallacious. The three systems are indeed so intimately interrelated that any interference with the physiology of one must necessarily affect the other systems either immediately and intensively or in minor degrees but accumulating into a major effect eventually. For instance, a massive cardiac infarct will depress myocardial function and diminish cardiac output, thus decreasing the amount of blood circulating through the pulmonary area to pick up oxygen. Administration of oxygen during this phase of the emergency will provide additional oxygen which will be absorbed by the plasma. A cerebral embolus or hemorrhage may so influence respiration as to diminish tidal and minute volume. Additional oxygen during this depressed respiratory phase will be of great value to the brain itself and to the cardiovascular system. It is in the initial 12 to 15 minutes when no immediate help is available that an oxygen therapy unit such as that described is most helpful. This period may be prolonged by changing tanks every 12 to 15 minutes.

It is not inconceivable that these units could be used in group emergencies, e. g., when a number of people are overcome by smoke or carbon monoxide. Additional oxygen in the plasma before better help arrives may mean the difference between survival and death. If a small nebulizing unit that can be worked with this unit is devised, it may even be employed in an acute asthmatic attack, provided the patient has not developed tolerance to the drug used.

The utility of this unit in chronic respiratory, cardiovascular, or central nervous system conditions is very limited. It may help in acute exacerbations of these chronic conditions if the patient is away from good, efficient therapy. If this unit is to be utilized efficiently, one must always remain aware of its limited period of effectiveness.

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The unit described was supplied by Emergox, Inc., Nashville, Tenn.

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EMBOLISM AT BIFURCATION OF AORTA

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Embolism at the aortic bifurcation is a serious emergency. The diagnosis is not difficult if the physician is aware of this possibility in patients with auricular fibrillation, mitral valvular disease, or recent myocardial infarction. Sudden pain in the back and in the extremities; shock, coldness, and numbness in the extremities, followed by cyanosis; and absent arterial pulsations are the usual symptoms and signs of this condition. Immediate heparinization to prevent progression of the thrombus and closure of collateral channels is probably the most important of all the conservative therapeutic measures. Embolectomy is the treatment of choice when the general condition of the patient will permit. It may be successful even at a late stage.

Peripheral arterial embolism is usually the result of clot formation within the chambers of a heart. In about 80% of the cases it is associated with auricular fibrillation or myocardial infarction, and in 20% it is the result of mitral stenosis, subacute bacterial endocarditis, pulmonary vein thrombosis, aneurysm of the aorta, and atheromatous plaques in the aorta. Occasionally a paradoxical embolus may originate in a thrombosed peripheral vein, pass to the right side of the heart and through a patent foramen ovale into the left ventricle, and then pass into the peripheral arterial system. This is extremely uncommon.

In a review of 330 cases of peripheral arterial embolism, Haimovici [1] found that 38% of the emboli lodged in the common femoral artery, 14% in the popliteal artery, 16% in the iliac artery, 9% at the bifurcation of the aorta, and 9% in the brachial artery. The remainder were scattered in the other peripheral arteries. Multiple individual emboli and "showers" of emboli are not uncommon. Albright and Leonard [2] studied 193 cases of aortic embolism gathered from the literature and found that 144 patients (74%) died as the result of the embolus, 26 were cured by embolectomy, 12 improved spontaneously or on conservative treatment, and 11 survived subsequent amputations.

About 40 to 60% of untreated patients with embolism of the major peripheral arteries will develop gangrene. With the advent of anticoagulants, sympathetic anesthetization, and the newer vasodilating drugs, this high incidence of limb mortality was reduced somewhat, but in many of the cases where gangrene was averted only a partially useful limb was obtained because of the residual circulatory impairment. Of all the sites of lodgement of peripheral arterial emboli the bifurcation of the aorta seems to be the most serious.

In 1895 Sabanieyeff [3] reported the surgical removal of a femoral embolus but was unsuccessful in preventing gangrene. In 1911 Labey [4] successfully removed a femoral embolus six hours after it occurred, and in 1913 Bauer [5] reported the first successful aortic embolectomy. Through the influence of Key [6] and other Scandinavian surgeons, interest in peripheral arterial emboli was stimulated, and since 1922 there has been a steadily growing literature on the subject. With the more frequent resort to embolectomy in the past 25 years the results have improved greatly with respect to the number of limbs saved and their usefulness. It is the consensus of opinion among surgeons now that, whenever the condition of the patient permits, early embolectomy is the treatment of choice when the embolus lodges in the aorta, iliac, femoral, popliteal, subclavian, axillary, brachial, or carotid arteries.

This report is based on personal experience with 23 cases of embolism at the aortic bifurcation. There were 14 females and 9 males whose ages ranged between 27 and 73 years. All had some form of heart disease. Eighteen patients had rheumatic heart disease. Of these, 17 had auricular fibrillation (1 also had subacute bacterial endocarditis) and 1 had mitral stenosis. In 14, the embolus occurred at home when the patient was fully compensated and seemingly well. Twelve were receiving maintenance doses of digitalis. Four patients developed the embolus while in the hospital; one was being digitalized because of cardiac decompensation; one was under treatment for subacute bacterial endocarditis; one developed the embolus four days after a hysterectomy from which she seemed to be recovering uneventfully; and one developed an aortic embolus while being studied for a possible renal embolus. Although peripheral arterial embolism has frequently been attributed to conversion of the cardiac rhythm by therapy with quinidine, it is interesting to note that none of these patients had been taking quinidine immediately prior to formation of the embolus. Five patients were in the hospital and being treated for acute myocardial infarction when the embolus occurred—7 hours, 12 hours, two days, two weeks, and three weeks after the acute coronary thrombosis.

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Clinical Findings

The onset of the embolism was sudden in all cases. In seven patients there was moderate to severe pain in the lumbosacral region or buttocks which quickly radiated down the thighs, simulating sciatica. In 16 the pain was limited to one or both legs. In all cases the acuteness of the pain disappeared in about 30 minutes, leaving a dull ache in the region of the calf muscles and numbness in the feet and legs. One patient collapsed because of the severe pain while walking outdoors, and three patients fell to the floor at home. All developed some degree of shock. In those patients with recent coronary thrombosis who were examined within a few minutes of the onset because they were in the hospital, the clinical picture of shock, with marked weakness, perspiration, a rapid pulse, and drop in blood pressure, simulated that of another myocardial infarction and would have been so diagnosed but for the pain in the extremities which directed attention to the peripheral arteries.

In most patients the extremities were very pale immediately after the onset, but a diffuse or mottled cyanosis of the feet and legs and coldness of the skin developed within 30 to 60 minutes. In several the cyanosis extended to the groins, and in two even the lower part of the abdomen became cyanotic after several hours. Numbness of the feet and legs developed in all cases but seldom extended as high as the cyanosis. Paralysis of the muscles of the foot and leg accompanied the sensory loss. The thigh muscles were seldom involved even when the cyanosis extended to the groin. In 20 patients no iliac, femoral, or distal arterial pulsation could be detected and the oscillometric readings were zero in the thighs and legs. In three a weak femoral pulse was present on one side.

In two of the patients the diagnosis was made at the time of hospitalization for gangrene one and two weeks later. In three the diagnosis was made at the time of hospitalization for cardiac decompensation two weeks, six weeks, and six months later respectively. In each there was a typical history of sudden collapse due to pain in the extremities followed by cyanosis, coldness, and both motor and sensory paralysis. The arterial pulsations in the extremities were absent when the patient entered the hospital. In two of these patients, one who died from the underlying heart disease and the other after a cerebral embolus, the diagnosis of aortic embolus was verified at postmortem examination by the presence of a recently organized embolus at the bifurcation without evidence of local atherosclerosis. Apparently in each of these three patients sufficient collateral circulation to maintain viability of the extremities developed spontaneously. None of these patients had been able to stand more than a few minutes or walk more than 25 to 50 steps without pain in the legs.

Diagnosis

The diagnosis of acute occlusion of the abdominal aorta by embolus is not difficult if the attending physician is aware of such a possibility in a patient with auricular fibrillation, mitral heart disease, or recent myocardial infarction. The shock-like state may simulate recent myocardial infarction, but the severe pain in the back and in the extremities associated with cyanosis and coldness in the extremities should direct attention to the peripheral circulatory problem. The absence of the femoral pulsations and zero oscillometric readings will establish the diagnosis of aortic or iliac occlusion. It is impossible to differentiate between aortic and bilateral iliac occlusion because the symptoms and objective findings are the same.

The differentiation between embolic occlusion and acute thrombosis of the abdominal aorta may be difficult at times because of the similarity of the clinical picture. The presence of auricular fibrillation, mitral heart disease, subacute endocarditis, or a history of recent myocardial infarction should indicate the diagnosis of embolism; the absence of these conditions, especially in a patient with other evidence of arteriosclerosis, is suggestive of thrombosis. In the latter type of case there is often a history of intermittent claudication for a long period before the acute episode, and occasionally calcification of the abdominal aorta may be visible in a roentgenogram, indicating long-standing aortic disease. A record of the condition of the peripheral arterial circulation before the acute episode is one of the best diagnostic aids. Such a record should be part of the medical chart of all patients with heart disease and of all elderly individuals.

A thoracic aortic aneurysm may occasionally be the origin of an embolus when a portion of the laminated thrombus with which it is usually lined breaks off. An abnormal pulsation of the chest wall or in the lower part of the neck and differences in the blood pressure determinations in the upper extremities should make one suspect that a thoracic aneurysm is present. A roentgenogram of the chest is usually diagnostic. An abdominal aortic aneurysm is more easily diagnosed. An expansile pulsating abdominal mass is usually present, and a lateral roentgenogram will often reveal the calcified wall of the aneurysm.

A dissecting aneurysm may also cause obliteration of the aortic bifurcation or of one or both iliac arteries. This condition is differentiated from an aortic embolus by the sudden excruciating and tearing pain in the back which radiates to the extremities. There is usually no auricular fibrillation or evidence of recent myocardial infarction. If the aneurysm originates in the chest, as is frequently the case, obliteration or narrowing of the mouths of the aortic branches will often result in motor and sensory disturbances and sometimes hemiplegia and coma. Hematuria may be present when the renal arteries

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are closed by the dissection in the aortic wall. When the iliac arteries are not completely occluded a weak pulsation may be detected in the femoral arteries.

Another condition which had been described by Atlas [7] and which I have encountered several times is severe spasm of the femoral and iliac arteries associated with embolism in the more distal vessels. Occasionally this can simulate organic high occlusion. One such case observed recently was that of a 38-year-old woman with auricular fibrillation of long standing who suddenly developed pain in the thighs followed by coldness and cyanosis of the extremities to the knees. The iliac and femoral pulses were absent, and the oscillometric readings were zero in the thighs and legs. Embolus at the aortic bifurcation was diagnosed. There was no improvement in the condition after seven to eight hours of intensive conservative treatment by her physician, including such measures as caudal anesthesia, intravenously given papaverine hydrochloride, use of heparin, and digitalization.

At operation a strong aortic pulsation was present to the bifurcation. Both iliac arteries were pulseless and hard and contracted to less than half their normal diameter. No clot was found when the aorta and the iliac arteries were opened. The femoral arteries were also in a state of spasm and free of clot when exposed in the thighs. A soft catheter was passed distally to the popliteal bifurcation on each side, 10 mg. of heparin solution was injected, and the arteriotomies were closed. Papaverine and heparin therapy was continued. Twelve hours later, both femoral pulses were present and the feet were warm but the popliteal and the pedal pulses were not obtainable and the oscillometric readings were markedly diminished. It is possible that in this case a small clot may have broken on the aortic bifurcation and was then carried distally in each extremity to occlude the popliteal arteries. The absent iliac and femoral arterial pulses were probably due to spasm resulting from the intimal injury.

Treatment and Results

Of the 23 patients studied, 3 spontaneously developed adequate collateral circulation at home to maintain viability of the limbs. Two patients entered the hospital with bilateral gangrene one and two weeks after the embolism occurred. They were almost moribund on admission and died shortly thereafter.

Eighteen patients were seen primarily for the aortic embolus. Of these, 11 were treated conservatively because they either had too poor a cardiac condition to be operated on or were unwilling to accept surgical treatment. Six of these patients died from cardiac decompensation aggravated by the toxemia from the extensive bilateral gangrene within three days to two weeks. One patient developed gangrene in one extremity but survived a subsequent amputation. Four patients developed sufficient collateral circulation to maintain viability of the limbs but continued to have symptoms of vascular insufficiency thereafter. One of these latter patients died three weeks later of progression of the previous myocardial infarction. The treatment in all of these cases consisted of lumbar sympathetic anesthetization, intravenously given heparin, and papaverine therapy. The extremities were wrapped in cotton or wool to maintain the body heat and kept in a somewhat dependent position. Rapid digitalization was carried out whenever indicated.

In seven patients the cardiac condition was good enough at the onset or after several hours of treatment to permit operation, and embolectomy was performed. In four of these, auricular fibrillation and cardiac decompensation was present, one patient had compensated auricular fibrillation but had suffered a renal embolus 10 days previously, one had auricular fibrillation and subacute bacterial endocarditis, and one was recovering from severe myocardial infarction which had occurred two weeks previously. Six patients were operated on within 8 hours after the embolus lodged in the aorta, and one was operated on 34 hours later. The peripheral arterial circulation had not improved in any of these patients on the conservative therapy in spite of great improvement in the cardiac status after rapid digitalization in those who were decompensated originally. There was improvement in all patients immediately after the embolectomy; the femoral and, in several cases, the pedal pulsations returned, and the feet became warm and pink. Three of these patients have remained alive and well with no residual impairment of the peripheral circulation, one died of cardiac decompensation 24 hours after embolectomy, one died of a second myocardial infarction 10 days later, one died of a cerebral embolus three weeks later, and one died of a cerebral embolus 4 months later.

All of the embolectomies were performed transabdominally with the patient under spinal or inhalation anesthesia. After the opening of the abdominal cavity through a midline incision, the small intestine should be gently displaced into the upper abdomen or placed in a plastic bag outside the abdominal cavity for better exposure of the aorta. The vessels can then be easily palpated and exposed by incising the posterior peritoneum. The aorta and the iliac arteries containing the embolus are hard and do not pulsate. The proximal and distal ends of the embolus can usually be outlined. Distally the iliac arteries are constricted but soft and also nonpulsating. At this point in the operation 10 mg. of heparin in 10 cc. of saline solution should be injected distally into each iliac artery and the vessel occluded

with a nontraumatizing spring clamp to prevent distal progression of a portion of the embolus should it fragment during the manipulation and extraction. The aorta above the embolus should then be gently separated from the vena cava and an aorta occlusion clamp applied without closing. If lumbar branches of the aorta are present below this clamp they should be ligated to prevent back bleeding into the isolated segment of the aorta when the embolus is removed.

A 2-cm. linear incision is then made over the embolus in the aorta and extended distally into the iliac artery containing the longest segment of the embolus. When this incision is spread the embolus usually will be flushed from the vessel by the strong proximal aortic beat. The surgeon must be ready to quickly close the aorta occlusion clamp to prevent excessive blood loss when the embolus is removed. It is also well to forewarn the anesthesiologist of a possible drop in blood pressure when the aorta is opened. The clamps on the iliac arteries should be temporarily opened separately to permit any remaining fragments of clot to be flushed out from below. The artery is closed by a continuous running suture through all layers with 00000 arterial silk, and all clamps are removed.

If the femoral pulsations are now present and strong, indicating complete clearing of the embolus from the pelvic vessels, the posterior peritoneum is sutured and the abdomen closed. Absence of a femoral pulsation indicates obstruction in the external iliac or common femoral artery by a fragment of the embolus or a secondary thrombus. In such case the vessel involved is exposed and an embolectomy performed. Both extremities should be examined also for emboli or thrombi in the region of the deep femoral artery, in Hunter's canal, and in the popliteal artery; when present these should be removed through separate incisions.

In two of the patients a typical anterior tibial syndrome developed postoperatively. In each a secondary thrombus had been present in the femoral artery and had been removed separately. It seems probable that a part of this clot extended into the anterior tibial artery and had been incompletely extracted through the femoral arteriotomy. It may be that insertion of a catheter into the anterior tibial artery and flushing it out from below, as has been recommended, could have prevented this complication.

The serious nature of an aortic embolus occurring in a patient with severe heart disease can be seen from the fact that 11 of the 23 patients died within two weeks as a result of the gangrene or of the heart condition or both and 2 died of subsequent cerebral emboli three weeks and four months later. Embolectomy improved the circulation and prevented gangrene but did not affect the basic heart disease or prevent subsequent embolism.

Multiple emboli are not uncommon and may occur before and after the aortic occlusion. In the 23 cases reported there were nine known other emboli in seven of the patients. Five of these occurred before the aortic embolus and four subsequent to it. There were five cerebral emboli, three of which were fatal. Two of the fatal cerebral emboli occurred three weeks and four months after successful aortic embolectomy while the patients were receiving adequate anticoagulant therapy. In another case an aortic embolus developed two weeks after a coronary thrombus while the patient was receiving large doses of heparin; 10 days after a successful embolectomy he developed a second and fatal coronary thrombosis also while receiving anticoagulants. It seems that complete reliance cannot be placed on anticoagulants to prevent thromboembolic complications. Since further embolization may occur, it is believed that auricular appendectomy and mitral commissurotomy should be strongly considered when the emboli are due to auricular fibrillation or mitral heart disease. This was performed in one of the patients two months after aortic embolectomy.

Summary

Twenty-three cases of embolism at the aortic bifurcation have been reviewed. The diagnosis of aortic embolism is not difficult if the physician is aware of such a possibility in all patients suffering from auricular fibrillation, mitral valvular disease, and recent myocardial infarction. Immediate heparinization to prevent progression of the thrombus and closure of the collateral channels is probably the most important of all the conservative therapeutic measures and if possible should be carried out even before the patient is transported to the hospital. Vasodilating drugs and lumbar sympathetic anesthetization have been of questionable value in some cases.

Three patients spontaneously developed adequate collateral circulation to maintain viability of the limbs; two patients entered the hospital with extensive gangrene and died shortly thereafter. Eleven patients were treated conservatively. Of these, six died of gangrene and the associated heart disease, four developed adequate collateral circulation to maintain viability of the limbs, and one developed gangrene of one limb which was subsequently amputated successfully. Transabdominal aortic embolectomy was performed in seven patients, and there was immediate improvement in all. The femoral and in some cases the pedal pulses returned and the feet became warm and pink. Three of the patients have remained alive and well, one died of cardiac decompensation 24 hours after embolectomy, one died of a second myocardial infarction 10 days later, and two died of cerebral emboli three weeks and four months later.

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Embolectomy is the treatment of choice in cases of embolism at the aortic bifurcation when the general condition of the patient will permit. It should be performed as soon as possible but may be successful even at a late stage.

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CLINICAL NOTES

PRACTICE OF FLUID THERAPY

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I propose to discuss practical, day-to-day problems of fluid therapy rather than high theory. Many of our failures in regard to fluid therapy are not the result of our failure to keep up with the latest advances. In a great many instances poor fluid therapy may be carried out because we do not activate long-established principles of good medical care as well as humane, diligent nursing and administrative practices. At the risk of belaboring what may seem to some to be a rather dubious or ill-advised point, I wish to emphasize this thesis further.

Please ask yourselves these questions: How often is the practice of fluid therapy impaired by inadequate history taking? How often is the practice jeopardized by hurried physical examination? How often is it given a black name by utterly inaccurate measurements of intake and output? How frequently do we neglect to take accurate daily measurements of body weight? How often are our best intentions endangered by hospital chemical laboratories which lack professional supervision and which, in many instances, can be shown to be unreliable? How often is the successful practice of fluid therapy impaired by insufficient attention to underlying illnesses?

I wish that these problems and pitfalls occurred only in the practice of fluid therapy. But I suspect that analogous situations obtain in regard to such daily matters as surgical operations, antibiotic therapy, proper diets, and many others.

Read in part before the First Oklahoma Colloquy on Advances in Medicine.

I shall try to concentrate our attention on three commonplace aspects of fluid therapy: (1) risks of air embolism; (2) the matter of how rapidly or slowly fluids should be given parenterally; and (3) the utility of accurate daily measurement of body weight, especially in bedfast patients.

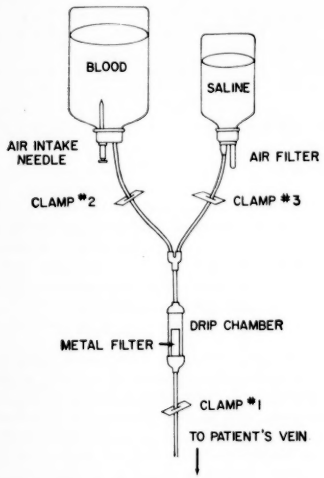
Risks of Air Embolism

At least one catastrophe at our hospital pointed an accusing finger at the risks of cavalier attention to standard equipment used daily for giving blood transfusions. The familiar Y-type set (see figure), as emphasized by Kerr,[1] is constructed with the built-in possibility of causing air embolism. Until Kerr's convincing demonstration of this possibility at our hospital I was ignorant of it. I am therefore bold enough to assume that this source of catastrophe has escaped the attention of many others as well.

Assume for the moment that the Y set pictured in the figure is intact, perfect in its manufacture, and without defects when used for transfusion. An infusion of blood is completed: clamp 2 remains open, clamp 1 is completely open, and clamp 3 constricts the tubing and controls the rate of saline administration. Under these circumstances large quantities of air can be shown to enter the tubing below the drip chamber at a rapid rate. The source of this air is the air-intake orifice of the empty blood bottle.

That this inrush of air occurs under the circumstances described above is readily verified by anyone curious enough to spend a little time manipulating the controlling clamps. The explanation for

this entry of air became clear to me through discussions with a biophysicist at our hospital, Dr. Clinton Janney. It can be shown that, when the blood bottle is empty, with clamps 1 and 2 open, and clamp 3 partially constricts the tubing, the pressure in the lumen above clamp 3 exceeds the atmospheric pressure. In sharp contrast, however, the pressure in the lumen below the constricting clamp 3 on the saline limb of the Y and below the junction with the blood side is distinctly less than atmospheric. These facts can be vividly verified by inserting a suitable needle into the lumen of the tubing above the constricting clamp 3; this results in an outpouring of saline solution, because the pressure within the lumen above clamp 3 is



Y-type blood transfusion administration set.

greater than the atmospheric pressure. But, if a needle is inserted into the lumen of the saline limb of the Y below the constricting clamp 3, numerous bubbles of air can be seen to enter, because the pressure within the lumen below clamp 3 is less than atmospheric. Air may enter from the empty blood limb of the Y because, when clamp 2 remains open, the pressure within the lumen of this limb is atmospheric (freely communicating through the air-intake needle), whereas the pressure at the junction of the Y (below the constricting clamp 3) is less than atmospheric.

A special, perhaps less obvious, example of the same conditions develops if the blood bottle is empty, clamp 2 is open, and clamp 3 constricts the tubing to a greater extent than clamp 1. Again, large quantities of air may enter the tubing below the drip chamber rapidly, and a similar explanation obtains.

A moral of this story is that, after the blood has run in, clamp 2 must obstruct the lumen completely, clamp 3 should be opened completely, and clamp 1 should constrict the lumen and control the infusion rate. Unfortunately, the clamps of leading manufacturers do not readily lend themselves to easy assessment of just how much they constrict the lumen. Invariably clamps such as a spring clamp or a hemostat at the upper limbs of the Y are far more effective and much less dangerous. Incidentally, instead of the throw-away clamps provided at position 1, a well-made tunnel or screw-type clamp is desirable for rate control. Furthermore, since in a sense an empty blood limb of the Y is precisely analogous to a needle poised to puncture the tubing, serious consideration of the advisability of abandoning Y sets appears to be in order.

Let us turn now to some of the risks of air embolism related to the use of defective sets for fluid administration. Holes may be present in the plastic tubing as a consequence of faulty manufacture, careless handling, or needle punctures. If the drip chamber and plastic tubing are fabricated as separate components there is danger of a leaky junction. Such defects may occur not only in Y sets but in single-channel sets as well.

It can be readily demonstrated that the position of the constricting clamp controlling the rate of fluid flow is of critical importance. For example, consider a single-channel set with a single fluid-control clamp. If the tubing is punctured above the constricting clamp, fluid leaks out. In contrast, if the puncture is below the constricting clamp, large quantities of air may enter the tubing and travel to the vein. The constricting clamp controlling flow should, therefore, be as close to the vein used for injection as possible. The fluid administration set should be tested for leaks prior to use.

The above discussion, admittedly incomplete, is intended to awaken interest (and vigilance) in air embolism as a significant hazard of fluid therapy. Additional information can be found in reviews by Kerr [1] and Bailey.[2]

Rates of Fluid Administration

"Morphine sulfate 15 mg. (h) p. r. n." If this order were to appear in the physician's order book of a well-run nursing station, the nurse would probably insist on a statement of how frequently the morphine may be given. Otherwise the order, as erroneously written, permits a rate of morphine injection of, for example, 15 mg. every five minutes.

"One liter of 10% glucose in isotonic saline i. v." Unfortunately this is the customary form of an order for intravenous administration of fluids and,

in this instance, the nurse will probably not insist on a statement of injection rate. Nevertheless, under certain circumstances, the intravenous injection of fluids at an improper rate may be as catastrophic as overly rapid administration of morphine.

A physician's order for parenteral administration of fluids which fails to specify the desired rate of flow, both in drops per minute and in cubic centimeters per hour, is written incorrectly. It should be a hospital rule that the fluid prescription include specifications for both of these rates. If these rate factors are omitted, or if they are included but not conscientiously enforced, the rate of fluid administration becomes a guesswork affair, inviting the serious consequences of too rapid or too slow infusion. It is something of a mystery why most of us consider it the physician's responsibility to decide on the quantity and composition of intravenously given fluid but, in effect, frequently evade the responsibility of selecting and enforcing an appropriate rate.

It is surprising how often, in attempting to exercise control over rate, the physician assumes that 1 cc. of fluid is equivalent to 15 drops. The number of drops in a given volume of fluid injected through an infusion drip chamber is determined primarily by the size of the orifice which delivers the fluid into the chamber. This orifice varies in size, depending on the manufacturer. For example, Abbott sets deliver about 20 drops per cubic centimeter of fluid, whereas Baxter sets deliver only 10 drops per cubic centimeter. Abbott has recently released a so-called microdrip set which provides 43 to 45 drops per cubic centimeter; the latter is useful for slow rates of flow, as in babies or children.

Control of the rate of flow is critically related to the character of the clamp used in constricting the tubing. Many of the disposable sets provided for parenteral administration of fluids by leading suppliers have clamps which require much time and effort to achieve precise adjustment of rate. Such clamps should be replaced by suitable screw or tunnel-type clamps. Nevertheless, not even the most precise clamp is a substitute for eternal vigilance since, unless the infusion rate is checked and, if necessary, adjusted at frequent intervals, rates of flow may undergo striking increase or decrease as a result of change of position of the extremity subjected to infusion, change in tone of the vein, or change in location of the needle.

I have seen several types of disaster which can be traced to lack of interest in rate control. Thus blood and other fluids given too fast to patients with diseases of the heart or lungs have produced pulmonary edema. Fluid administered too slowly has failed to remedy dehydration and mineral deficits. Dextrose and other hexoses injected too rapidly have resulted in self-defeating melituria, osmotic diuresis, and increased urinary loss of electrolytes. Infrequent observation of the rate of flow has caused "runaways"; this is particularly unforgivable and tragic in infants and children. When one delves into the causes of such errors it may be apparent that the prescribing physician had intended that the fluid be given at a proper rate. In this sense the catastrophe may be regarded as a failure of the physician to translate intention into actuality.

An atmosphere of cooperation and understanding must be cultivated in each hospital in regard to this matter of rate control. Thus nurses, house staff, attendants, and attending physicians must come to appreciate the importance of enforcing prescribed rates of flow 24 hours a day and seven days a week. Their appreciation of this can come from checks on flow in the course of fluid therapy in a given patient, as well as from conversations, lectures, demonstrations, memoranda, and ground rules. Adequate quality and quantity of personnel and facilities are obvious prerequisites. The practical aspects and plans are best analyzed on an individual basis, taking into account the peculiarities of the individual hospital.

There are all too few rules of thumb which I can proffer in regard to exactly which rate of flow should be selected for a given situation. Among usually recognized factors which must be taken into consideration are type and quantity of fluid prescribed; technical matters such as availability of veins; comfort of the patient; continuous prevention of ketosis; status of heart, lungs, and kidneys; and rates of dextrose utilization. The latter is probably less than 0.3 Gm. of dextrose per kilogram of body weight per hour in the starved subject because of "starvation diabetes." In the hydrated, nonstarved subject, a safe figure is probably less than 0.5 or 0.6 Gm. per kilogram of body weight per hour. It is useful to test the urine for sugar at regular intervals. If glycosuria is less than 3+ it is probably of little importance in causing wastage of water and electrolytes.

Accurate Daily Measurement of Body Weight

How much fluid shall I prescribe for this patient during the next 24 hours? This is one of the burning questions each clinician strives to answer satisfactorily as he treats patients with parenteral administration of fluids. A valuable help in answering this question is afforded by knowing whether the water stores of the patient have increased, decreased, or remained unchanged. A simple example is the patient who on day one is assumed to have a normal quantity of body water, and who 24 hours later is found to have sustained a net loss of body water approximating 2 liters. The crux of the matter is that estimates of change

in the quantity of body water are best and most accurately made by serial (usually daily) measurement of body weight.

Medical history, physical examination, chemical and other laboratory data, measurement of intake and output, knowledge of underlying illness—all are highly significant, invaluable contributions to successful fluid therapy. But, useful and crucial though they may be, none holds a candle to the utility of serial body weights in reflecting day-to-day changes in body water. And a bit of reflection should show that knowledge of change in body water is one of the principal determinants of the answer to the question: How much fluid is appropriate for the next 24-hour period?

It can be reasonably assumed, for purposes of fluid therapy, that about 0.1 to 0.4 kg. (4 to 14 oz.) of body weight is the range of daily loss in an adult sustained on parenterally administered fluids, provided that no deficiency of body water has developed. The extent of this non-water component of weight change depends on the balance between caloric intake and caloric need. This balance may vary considerably. But even if the caloric intake is negligible non-water loss should fall within 0.4 kg. if adequate fluids are provided. For example, if accurate body weights show that a patient has lost 0.3 kg. (11 oz.) of weight in 24 hours, an insignificant change in body water can be inferred. On the other hand, if the authentic 24-hour weight loss is 2.3 kg. (5 lb.), a decrease in body water of about 2 liters is suggested.

This estimate of change in body water is most readily inferred from change in weight, rather than from other information which can be brought to bear on the problem. Thus, consider a patient who on day one is normally hydrated and weighs 60.0 kg. (132.0 lb.) and whose body weight is 59.7 kg. (131.5 lb.) on day two, 59.7 kg. (131.5 lb.) on day three, and 59.4 kg. (131 lb.) on day four—showing a daily loss of body weight of less than 0.4 kg. (14 oz.). Assuming that this patient is losing fluid from the gastrointestinal tract over the next few days and that parenterally administered fluids are the exclusive source of intake, we can safely assume that this daily loss in body weight of less than 0.4 kg. (14 oz.) does not represent a significant change in the total quantity of body water. Suppose, however, that the weight were found to be 57.7 kg. (127.3 lb.) instead of 59.7 kg. (131.5 lb.) on day two. This loss of 2.3 kg. (5 lb.) would define a deficit of body water of about 2 liters.

How readily can this 24-hour loss of 2 liters of body water be detected by means other than serial measurement of body weight? The clinical history and physical findings during this 24-hour period would at best yield useful qualitative information. Accurate measurement of intake and output is an indispensable component of optimal fluid therapy. Even such measurement, however, does not include variable loss of water through skin and respiration. Nor are accurate measurements of output of fluid usually available to the clinician. Moreover, certain types of gastrointestinal losses, for example profuse drainage from a fistula, vomiting, and diarrhea, lend themselves poorly to quantitative collection. Hence measurable intake and output are unworthy substitutes for serial body weights in relation to change in body water. As already emphasized, however, serial body weights do not yield the vital information gleaned from knowledge of intake and output. The latter data are useful in judging the composition of replacement fluids; body weight change sheds no light on this problem.

Laboratory data generally available in hospitals, although crucial for many aspects of fluid therapy, would yield no more than a clue concerning the 2-liter deficit of water. Such measurements would not quantitate the deficit to the extent derived from change in body weight unless direct, ordinarily unavailable, serial measurements of body water were undertaken.

The above reasoning establishes the supremacy of serial measurement of body weight in estimating change in body water and thus in helping to guide the quantity of fluid prescribed. At the same time, body weights are not proper substitutes for clinical history, physical examination, laboratory data, and measurements of intake and outgo. These have their own special utility and, although beyond the scope of this presentation, all must be taken into account in devising a proper fluid prescription.

Two major problems appear to conspire against obtaining body weight measurements which are meaningful for fluid therapy: First, the bedfast patient is frequently not weighed because of alleged technical difficulties. This fact is in a sense tantamount to stating that the more serious the illness the less the need for objective criteria to guide fluid therapy. There is at least one commercially available scale [3] which facilitates weighing of bedfast patients. Secondly, many measurements of body weight are about as useful as no measurements at all. This is true because of the grim fact that body weights as ordinarily measured in hospitals are subject to gross inaccuracy. This then resembles the situation in regard to accurate intake and output data, save for the fact that obtaining a precise body weight is intrinsically simpler and less demanding of time and effort.

Weighing a patient with a blanket on one day and without this blanket 24 hours later may be reported as a loss of body weight of 2 kg. (4.4 lb.) or more. This apparent loss of body water could lead to disastrous treatment. Physicians charged

with the responsibility of fluid therapy have by this very fact accepted the responsibility for providing a carefully thought-out, continuously supervised program of body weight measurements which meets the needs of their individual hospitals. Even those prescribing fluids for infants and children often ignore the comparatively simple problem of arranging for accurate body weights and evidently prefer instead a kind of roulette-wheel guidance. Is it unreasonable to suggest that an era in which gargantuan feats in the operating room are almost commonplace should also be characterized by the ease with which accurate body weights can be obtained and interpreted?

666 Elm St. (3).

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COUNCIL ON DRUGS

Report of the Council

The Council has authorized publication of the following report.

H. D. Kautz, M.D., *Secretary.*

PENICILLIN AND OTHER ANTIBIOTICS IN MILK

Widespread use, by dairy farmers, of animal antibiotic preparations, notably penicillin, which are commercially available for intramammary treatment of bovine mastitis, has led to the frequent occurrence of detectable amounts of penicillin and other antibiotic components in milk distributed for human consumption. The presence of penicillin and other antibiotics in consumer milk arises chiefly from the failure of some dairy farmers to withhold from marketing the milk of animals treated for mastitis until such preparations have been completely eliminated from the udders. There is also some suspicion that the preparations are being used promiscuously in healthy dairy herds or are being directly added to milk as a preservative against spoilage during warm weather. The significance of penicillin in the milk supply devolves chiefly around the question of its potentiality to cause allergic reactions in previously sensitized persons or to sensitize previously nonallergic individuals.

Penicillin preparations for use in the local treatment of bovine mastitis were first certified for direct sale to dairy farmers in 1947 by the Food and Drug Administration. In 1951 this agency instituted a regulation requiring the printed matter accompanying such preparations to bear the statement, "Important: Milk from treated segments of udders should be discarded or used for purposes other than human consumption for at least 72 hours after the last treatment." The FDA subsequently found that, although repeated doses of 25,000 units of penicillin for each infected segment of the udder were usually considered adequate for effective treatment of mastitis caused by penicillin-susceptible micro-organisms, competition among manufacturers had gradually resulted in an increase in the potency of some preparations to as much as 1,500,000 units per dose. Such highly potent products were considered likely to increase the length of time required for complete elimination of the antibiotic from the milk of treated animals, whereas there was no evidence to indicate that massive doses would increase the efficacy of the drug. Accordingly and on the basis of three nationwide surveys which showed that collected and tested samples of market milk contained variable small amounts of penicillin, the FDA held a conference with representatives of all interested groups and a panel of medical authorities on antibiotics, allergy, and pediatrics to consider the potential health hazard of exposure to antibiotics in market milk. It was the consensus of this panel that antibiotics such as bacitracin, neomycin, polymyxin B, and the tetracyclines, all of which may be found in mastitis preparations, do not pose a hazard to health, even though they might find their way into market milk. On the other hand, it was agreed that even in the small amounts present in milk, penicillin, which is highly antigenic, is capable of causing allergic reactions in highly sensitive individuals. It was estimated that the number of such persons comprised something less than 10% (17 million) of the total population and that the reactions to penicillin in milk could vary from mildly transient to possibly serious ones.

Early in 1957, the FDA published in the *Federal Register* its intention to limit the labeling directions for use of penicillin mastitis preparations to 100,000

units per dose. The chief opposing arguments to this proposal were (1) that penicillin could be excluded from milk without reducing unit dosage by incorporating a nontoxic dye in mastitis preparations to color milk from recently treated animals and (2) that the public health would be protected by restricting use of the preparations to prescription by licensed veterinarians. Both of these alternatives were overruled by the FDA because no assuredly nontoxic dye suitable for the suggested purpose was available and because restriction for use only by prescription of veterinarians would involve extra expense and possible hardship to dairy farmers due to the inaccessibility to veterinarians in some localities, plus the fact that, under the law, adequate directions for lay use could be written for use of mastitis preparations. Accordingly, federal labeling regulations were amended and became effective respectively as follows in July and August of 1957: The immediate containers, rather than the package literature, of preparations intended for the treatment or prevention of mastitis in dairy animals, are required to bear the statement, "Warning—Milk taken from dairy animals within ..... hours after the latest treatment for mastitis must not be used for human consumption." (The blank is to be filled in with the number 72 unless proof is furnished to justify a shorter period for a particular preparation.) The directions in the labeling for such use of penicillin preparations are required to specify single doses not to exceed 100,000 units. In cooperation with the U. S. Department of Agriculture, the FDA also undertook an intensive program to educate farmers through the National Milk Producers Federation concerning the importance of not using milk for human consumption from cows treated for mastitis for a period of three days after the last treatment. The FDA has indicated that, if the current regulations and educational program are not adequate to eliminate penicillin from the milk supply, it may become necessary to prohibit its use in animal mastitis preparations.

The American Veterinary Medical Association has expressed the view that there is an adequate number of veterinarians to supervise and provide this form of local treatment for mastitis and that penicillin is the drug of choice in treating certain forms of bovine mastitis. In its opinion, elimination of penicillin for this purpose would constitute unwarranted interference with veterinary service, whereas restriction of penicillin to a professional level would eliminate almost entirely the abuses now observed.

The majority of a representative group of allergists, whose opinions were sought regarding the current status of the problem of allergic reactions to penicillin-contaminated milk, are in substantial agreement that such reactions have occurred and probably have gone undetected in a larger number of instances than is reflected by reports in the medical literature.[1] Some allergists have not encountered such reactions; others have seen reactions after ingestion of milk, which suggested sensitivity to penicillin. A few are inclined to the view that the small amounts of penicillin found in milk are harmless to penicillin-sensitive persons except in the rare, exceptionally sensitive individual. As little as 2 to 3 units of ingested penicillin have produced an immediate anaphylactic type of reaction in extremely sensitive persons. Recent experiments also have shown that an oral dose two to three times the intravenous dose is required to produce reactions in subjects whose skin has been passively sensitized by injections with serum which contains antibodies to penicillin.

Most of the allergists consulted who have observed reactions ascribed to penicillin in milk indicate that these are usually of the commonly encountered, delayed type of chronic or recurrent urticaria. A minority of the consultants believe that definite clinical proof is available to show that immediate and delayed reactions are caused by penicillin in milk and that, although the incidence of penicillin contamination of milk samples is declining, the problem of allergy is increasing as a greater portion of the population becomes sensitized to penicillin. There appears to be more uncertainty regarding the capability of the small amounts of penicillin in milk to induce penicillin sensitivity than to produce reactions in persons already sensitive to the drug. However, in certain studies of rheumatic fever, considerable information is available relative to the development of sensitization to orally and subcutaneously administered penicillin. One consultant has suggested the possibility of limiting penicillin therapy of mastitis in dairy animals to systemically injected soluble preparations of the drug, as a means of avoiding the contamination of milk. The further suggestion that testing procedures be established for detection of penicillin in market milk would be very difficult to carry out with the techniques for testing which are now available, particularly at the level of local milk receiving centers.

Summary and Conclusions

The failure of some dairy farmers to withhold from the market milk from animals that have been recently treated for mastitis by intramammary infusion of penicillin preparations sold directly for this purpose, together with their abuse of such preparations in healthy dairy herds or as preservatives by direct addition to milk, has created a public health problem by exposure of consumers who are allergic, or may be sensitized, to variable small amounts of penicillin in the milk supply. The presence in milk of other antibiotics arising from similar use and abuse of such preparations does not appear to constitute a similar hazard.

Current federal labeling regulations require that animal antibiotic preparations intended for lay use for the prevention and treatment of mastitis by local intramammary infusion be sold with a warning on the container against human consumption of milk from treated animals up to 72 hours after the last treatment and that penicillin preparations intended for this purpose be sold with directions for use of single doses not to exceed 100,000 units each.

There is presumptive, if not conclusive, evidence that ingestion of penicillin-contaminated milk has produced, and is capable of producing, immediate and delayed generalized allergic reactions in persons highly sensitive to this antibiotic and that, although comparatively rare, reactions attributable to this source have probably gone unreported or unrecognized. The potentiality of ingested penicillin in milk to induce penicillin sensitivity in nonallergic individuals is suspected but not established.

There does not appear to be adequate evidence to prohibit totally the use in animals of antibiotics to which bacterial resistance may develop and which may be considered essential for treating human infections.

On the basis of available evidence of its oral allergenicity, such further measures as may be required to completely eliminate penicillin from the milk supply should be undertaken by the U. S. Department of Health, Education, and Welfare. The elimination of other antibiotic contaminants of milk, although desirable, appears to be less urgent.

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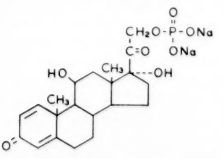
NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Prednisolone Phosphate Sodium (Hydeltrasol).—Sodium prednisolone 21-phosphate.—The disodium salt of 21-prednisolone phosphoric acid.—The structural formula of prednisolone phosphate sodium may be represented as follows:



Actions and Uses.—Prednisolone phosphate sodium is an inorganic ester of prednisolone, with the same intrinsic properties and the same hormonal effects as the parent gluco-corticoid. It is more soluble than prednisolone or its acetate and butylacetate esters. When given parenterally, it has a rapid onset and short duration of action. Although prednisolone phosphate sodium is the disodium salt of 21-prednisolone phosphoric acid, the usual therapeutic doses do not contain enough sodium to have a significant effect on daily salt intake. Each cubic centimeter of the injectable solution contains 20 mg. of steroid but only 4.9 mg. of sodium. (See the general statement on gluco-corticoids in New and Nonofficial Drugs.)

Prednisolone phosphate sodium is used for topical, ophthalmic, and parenteral administration for the management of conditions amenable to gluco-corticoid therapy.

An aqueous solution of prednisolone phosphate sodium may be injected intramuscularly or intravenously for the initial management of emergency situations in which intense systemic corticoid therapy is indicated. Because of the rapidity with which prednisolone phosphate sodium is absorbed from the site of intramuscular injection, this route is preferred to intravenous injection except in the gravest situations. Once the initial emergency situation is under control, steroid maintenance is best accomplished with oral medication or with a longer acting parenteral preparation.

Prednisolone phosphate sodium may be given by intrasynovial (intra-articular and intrabursal) and periarticular injection for the treatment of painful disorders of the joints, tendons, bursae, and nerve sheaths which are usually responsive to the anti-inflammatory action of the gluco-corticoids. The drug may also be used by local injection for the treatment of ganglion and soft tissue inflammations. By any of these routes, the effects are primarily local; i. e., systemic steroid effects are not likely to occur. Local injection of the drug usually affords relief of symptoms within two hours. After intra-articular injection, this relief is of short duration, generally no more than 48 hours. After soft tissue injection, however, relief of symptoms is more durable and may last a few days to a few weeks. For local injection, the drug is best given with one of the other less soluble but longer acting steroids available for intrasynovial and soft tissue administration. None of these drugs should be used for the injection of intervertebral joints.

Topical preparations of prednisolone phosphate sodium are available for the treatment of those acute or chronic dermatoses that have an allergic or inflammatory basis and, frequently, associated pruritus. The drug may also be expected to provide some relief from pain associated with the acute inflammatory phase of sunburn and insect bite. Use of this drug in the management of most dermatoses produces results similar to those obtained with other steroid compounds used topically.

Topically applied prednisolone phosphate sodium has been used to suppress inflammatory disorders of the anterior segment of the eye. As with any other steroid, the drug may control the inflammatory and exudative phase of certain eye diseases, but it does not affect the basic cause of the inflammation. Hence, best results can be anticipated in self-limited lesions in which such therapy suppresses the destructive phase of the disease and in chronic disorders in which the inflammatory process, especially the exudative phase, threatens the functional integrity of the eye. Stubborn cases of anterior segment eye disease may necessitate institution of systemic gluco-corticoid therapy; such therapy is always necessary when deeper ocular structures are involved. There are no reasons to suspect systemic steroid effects after the instillation of prednisolone phosphate sodium in the eye. The irritating effect that is sometimes produced in the eye by steroid ophthalmic suspensions is not a problem with the ophthalmic solution of prednisolone phosphate sodium because steroid particles do not form clumps when they are in solution.

Prednisolone phosphate sodium is capable of producing all the side-effects and untoward reactions characteristic of gluco-corticoids in general. Hence, it must be used with the same discretion as other drugs of this class. When used by the intramuscular or intravenous routes, especially in large doses or for prolonged periods of time, particular care must be exercised to guard against adverse systemic steroid effects. Topical administration of the drug may enhance preexisting or incipient skin infections. Neither topical nor ophthalmic preparations of the drug should be used in the presence of tuberculosis of the skin or eye respectively. As with any other steroid, the drug is absolutely contraindicated in patients with herpes simplex of the eye or adjacent skin.

Dosage.—Prednisolone phosphate sodium is administered by intramuscular, intravenous, intrasynovial, and soft tissue injection and topically to the skin, eye, or external ear.

For systemic use by either the intramuscular or intravenous routes, the dose varies from 10 to 100 mg. Since these routes are usually employed in emergency situations, amount and frequency of administration depend upon the severity of the situation and the response of the individual patient. In most cases, however, the total daily dose usually should not exceed 400 mg. Maintenance of systemic therapy with prednisolone phosphate sodium, if indicated, is usually accomplished by the injection of 10 or 20 mg. at intervals of three or four hours.

For intrasynovial (intra-articular and intrabursal) and soft tissue injection, the dosage and interval between injections depend upon such factors as the size of the joint, degree of inflammation, and the individual response of the patient. Prior to injection, the site may be infiltrated with a local anesthetic if necessary. For large joints such as the knee, the usual dose is 10 to 20 mg.; for smaller joints, 5 mg. may be sufficient. A dose of 10 to 15 mg. is used in most forms of bursitis. In inflammatory conditions of the tendons, doses of 2 to 5 mg. are used. For soft tissue infiltration and the treatment of ganglions, the dosage ranges from 5 to 30 mg.

For topical administration, a 0.5% preparation is applied to the affected areas of skin or the aural canal two or three times daily.

For ophthalmic use, one or two drops of a 0.5% solution are instilled into the conjunctival sac every hour during the day and every two hours during the night. When a favorable response has been obtained, dosage is reduced to one drop every four hours. Alternatively, a thin coating of a 0.25% ophthalmic ointment may be applied three or four times daily until a satisfactory response is observed. Thereafter, the ointment is applied once or twice a day. Since the ointment provides more prolonged medication, its use at bedtime in place of the solution may prevent disturbing patients' sleep by the need for repeated medication.

Preparations.—lotion (topical) 0.5%; ointment (ophthalmic) 0.25%; ointment (topical) 0.5%; solution (injection) 20 mg. in 1 cc.; solution (ophthalmic) 0.5%.

Year of introduction: 1957.

Merck Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of prednisolone phosphate sodium.

Use of Dextran in Nephrosis

The Council has reviewed the available evidence concerning the intravenous use of dextran solutions as an adjunct in the management of nephrosis. Solutions of dextran suitable for this purpose are hyperoncotic solutions of 12% concentration in distilled water. The 6% solutions of dextran in isotonic sodium chloride, which are suitable for the treatment of shock and are described in New and Nonofficial Drugs, are not suitable for use in nephrosis.

It is postulated that the intravenous injection of hyperoncotic solutions of dextran results in a mobilization of interstitial fluid, which is then excreted by the kidneys. Clinical trial reveals that 12% dextran solutions do, in fact, produce diuresis and consequent loss of fluid in some patients. The beneficial effects are temporary and are not necessarily greater than, or as much as, might be expected from other diuretic procedures. Elimination of fluid can sometimes be achieved with dextran, however, when the patient is refractory to other drugs. Dextran infusions are often more effective when used in conjunction with other edema-reducing agents than when used alone; moreover, the effects of these agents may themselves be intensified or enhanced if dextran is administered concomitantly or subsequently. Accordingly, dextran is to be regarded as an adjunct in the general management of nephrosis and should be used only in conjunction with other appropriate therapeutic measures.

It should be recalled that injection of dextran may produce a number of undesirable effects. An increase in bleeding time occurs in a substantial number of patients. This increase may not be apparent immediately after an infusion and may appear only after three to nine hours. In one study, the proportion of subjects showing measurable increase ranged from 31 to 100% for various commercial dextran preparations; the average for the entire series was 42%; in 8% of the subjects the bleeding time exceeded 30 minutes. The significance of this increase in bleeding time is not clear; although epistaxis, hematemesis, hematuria, and postoperative bleeding have occurred, excessive bleeding in surgical patients is uncommon. Until further experience is acquired, patients with a known bleeding tendency or those to whom large transfusions of whole blood have recently been given probably should not be regarded as subjects of choice for dextran administration.

In addition, dextran has the apparently inherent tendency to produce reactions of an antigen-antibody type in certain human subjects. Such reactions are of low incidence and mild character in adequately hydrolyzed and refined preparations, which provide an average molecular size approximating that of serum albumin. Infusions of 12% solutions in children have been reported to cause mild hypertension, associated with headache, nausea, and abdominal pain. Patients with myocardial disease, pulmonary edema, congestive heart failure, or overt uremia may be made worse by dextran administration.

For inducing loss of fluid in nephrosis, a 12% solution of dextran in distilled water is infused intravenously. The dose must be adjusted to the response of the individual patient. Infusion of 10 to 15 cc. per kilogram of body weight, administered daily for a minimum of three to five days, may be tried. The rate of administration should be 2 to 4 cc. per minute. Frequent determination of venous pressure during infusion is a salutary precaution.

All patients receiving dextran infusions, and particularly those with cardiovascular disease, should be carefully watched for signs of pulmonary edema or congestive heart failure. Should such signs appear, the infusion must be stopped immediately.

The Council voted to amend New and Nonofficial Drugs to describe the use of 12% dextran in nephrosis.

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of this additional use of dextran.

PREDISPOSITION TO PERNICIOUS ANEMIA.—One hundred and six relatives of 34 patients with pernicious anemia were tested for their ability to absorb tracer doses of Co^{60}-vitamin B_{12} by the method of Schilling. Ninety-seven healthy control subjects were similarly studied. A significantly greater proportion of the family members than of the controls had low test results. There was also a highly significant increase in the number of family members with abnormally low vitamin B_{12} absorption with increasing age. The control group showed no significant variation in the results of the Schilling test with age. . . . The data indicate that predisposition to pernicious anemia is inherited, most probably as the effect of a single dominant autosomal factor.—P. A. McIntyre, M.D., R. Hahn, M.D., C. L. Conley, M.D., and B. Glass, M.D., Genetic Factors in Predisposition to Pernicious Anemia, *Bulletin of the Johns Hopkins Hospital*, June, 1959.

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FIRST AID AND TRANSPORTATION FOR PATIENTS WITH SPINAL CORD INJURIES

GUEST EDITORIAL

Leslie W. Freeman, M.D., Ph.D.

THE recent tragic events leading to the incapacity of a great athlete with the subsequent rehabilitation program which led to his return to an active capacity with the Los Angeles Dodgers have served to focus renewed interest on spinal cord injuries. Most practitioners of medicine became acquainted with the problem during their student days, when these patients were considered to have a hopeless prognosis. Urinary sepsis, decubitus ulceration, and severe flexor spasms were some of the complications which caused the early death of almost every patient. However, the antibiotics, tidal drainage, blood transfusion, techniques of rehabilitation, and other developments have brought about a complete change in the outlook for these patients. Indeed, it is rare that one of these patients who lives to reach a medical facility equipped for specialized care will die as a result of the paraplegia alone. However, the incidents surrounding the early handling of the patient may well determine the ultimate functional result that can be expected.

It is highly unlikely that a patient will survive initial trauma severe enough to transect the spinal cord if the injury is a closed one. Thus, the injuries most usually grade from some point below an anatomic transection down to mere physiological interruption of the flow of impulses. Data evolved in the past 15 years would indicate that surprising degrees of function can be attained with relatively minor amounts of intact neural tissue. As such it is the responsibility of those who first contact and transport the patient to insure that the measures utilized do not add to the already existing neural damage.

Certain rules are of assistance in this regard. All unconscious patients or patients complaining of back or neck pain should be treated as though there were an injury to the spinal cord.[1] In this way, many patients with combined injuries may be spared the complete transverse traumatic myelitis which may be imposed on them by over-solicitous attendants at the site of the accident. Numerous cases are on record where the symptoms demonstrated have been exaggerated by improper handling. Fortunately, most patients with injury to the contents of the spinal canal are conscious. Questioning will usually bring out the presence of paralysis and loss of sensation. This can be verified by pinching the skin to establish the probable level of the lesion, bearing in mind that the arms can often be moved and felt in the lateral aspects (but not in the medial portions) in most persons surviving with cervical injuries. This initial neurological survey readily permits one to decide what special methods for initial care and transportation are required.

When a patient dives into shallow water, is involved in a vehicular accident, or suffers a fall, his initial attendance is most often conducted by uninformed personnel. Under many circumstances the extraction of the patient from the life-threatening situation may be conducted without regard to the type or site of injury. Even then it is amazing how frequently the responses of those involved may be directed instinctively toward proper handling. The majority of injuries to the spinal cord occur in the cervical or dorsolumbar regions. Modern first-aid classes have served to educate a great portion of the public to the hazards of uninformed activity in the face of calamity. As such, physicians often reach the site of accident with the patient impressed in the original position. Once the lesion is established or suspected every effort should be made to avoid rotation or flexion of the spine since the injury almost invariably has resulted from fracture and/or dislocation of the vertebrae. He should be moved "in one piece" without change in the vertebral alignment. The accomplishment of such a removal may require the utmost ingenuity. Boards, sticks, rolls of newspapers, overcoats, blankets, or other similar items can be utilized to achieve this end. The patient must never be transported in a sitting or semireclining position. If the patient can move his hands but not his legs, his injury is in the thoracic or lumbar region of the spinal cord or cauda equina. If the injury is such that the patient is unable to move his hands, he has cervical spinal cord injury, and the head and neck must be kept in perfect alignment during movement.

Professor of Surgery, Indiana University School of Medicine, Indianapolis.

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When it is established that the injury is below the neck, enough people should be present to lift the patient in such a way that the spinal alignment is not changed, and he should be placed on a stretcher (which might have to be improvised) fully extended with the face down. This position of natural extension may be sufficient to give bony realignment. One must remember that the bony injury is distinctly secondary to the neural damage and should receive only minor initial consideration except in regard to the possibility of invoking further damage to the neural structures. When the hands are also involved the most convenient method for immobilization of the head and neck is the application of a tapered roll of heavy cloth or similar material. This cloth should be wrapped about the neck continuously until the bundle comes to the jutting end of the chin. If the neck is in a flexed position, careful traction should be used with the hands under the angle of the jaw with a slow pull to an extended position before the application of the cloth splint. The patient needs someone to prevent flexion or rotation during movement and transportation. He should be transported recumbent in the face-up position and might need a blanket or coat under the shoulders to insure slight extension.

All authorities agree that persons with thoracic and lumbar injuries should be transported in the face-down position. There is some difference of opinion as to the transportation of persons with cervical injuries in the face-up position. One point raised against this position involves the possible aspiration of vomitus in intoxicated patients. The assessment of this potential can be anticipated and is not frequent enough to entertain as a standard consideration. In the face-up position, the patient who already has severely embarrassed respirations as a result of paralysis of the thoracic musculature is not further embarrassed by compression of the abdomen and consequent diminution of the excursions of the diaphragm. Furthermore, an adequate airway is difficult to establish with the patient in the face-down position unless the head is turned to one side—which would obviously be contraindicated. In the face-up position it is easier to maintain traction and extension. Under no circumstances should narcotics be administered to these patients unless other injuries dictate their use.

The vigilance exercised in the initial stages should be continued on admission of the patient to the hospital. If possible, word should be sent ahead to the hospital indicating the probable time of arrival. It is important to handle the situation as the most dire of emergencies, for the spinal cord does not usually recover from the effects of prolonged compression by bone, blood, or edema. Many patients benefit from immediate laminectomy,[2] and it would be well to have someone available to perform this operation shortly after admission of the patient to the hospital. It is imperative that catheterization of the bladder, with use of aseptic technique, be carried out at once. A note should be kept of the amount of urine obtained, and the urine should be examined for blood to detect direct injury to the urinary tract. The catheter should be anchored and should be no larger than 16 French.

Under personal supervision of the physician, preferably without the patient being moved from the stretcher, simple roentgenographic examination of the probable site of injury is the next step. In the interim, a rather complete physical examination should be made. The blood pressure is usually low, but one should not be misled into making a diagnosis of shock on this finding alone. Surgical or traumatic shock is never present in a person with uncomplicated spinal cord injury. Many patients have been denied possible surgical benefits because of a mistaken diagnosis of shock based solely on the finding of a low blood pressure level without the more essential signs of shock.

Immediate laminectomy and débridement, or other procedures dictated by the findings at operation, are desirable. On the other hand, experience in this procedure is mandatory, for it requires little in the way of operative trauma to produce an irreversible complete paraplegia. Mere inspection of the traumatic site offers little more than does blind manipulation—both of which often may be worse than no treatment at all. Closed manipulation for bone realignment has no place in the treatment of spinal cord injury. Many patients with good bony alignment never have return of function, and, conversely, many who have poor bony alignment show return of function. It is merely a question of whether the spinal cord axons have sufficient room within the spinal canal and whether the cord is entered by bony spicules or compressed by protruded intervertebral disk material or bone.

Roentgenograms fail to give complete evidence as to the degree of neural damage and should not be relied on for prognosis. One need only reduce one fracture—dislocation under direct vision and control—to understand how easily closed manipulative trauma might aggravate the initial injury. Furthermore, the mere fact that spinal fluid will flow from the small bore needle inserted into the spinal subarachnoid space below the level of the lesion means no more than that there is at least this large a passage for the flow of spinal fluid.[3] It gives no information about the situation at all points in the circumference of the lesion. Complete spinal fluid block means only that the space remaining in the spinal canal is smaller than the bore of the needle. This results only rarely from bony encroachment alone. It can result from pressure by protruded intervertebral disk material, ligamentum flavum, muscle trapped in recoil, extradural or intradural blood, pulpified cord tissue, edema of the cord, rupture of the dura, or some combination of these with the bony displacement or bony spicules.

Some exception to this firm view must be presented. In the lower lumbar region, only spinal nerve roots are present, and closed manipulation stands little chance of adding damage. On the other hand, injury to the spinal nerve roots is similar to peripheral nerve injury and should be treated as such. Newer procedures allow suture of severed spinal nerve roots. Successful suturing with functional return has been observed.[4] Débridement of blood and foreign tissue alone, with closure of dural tears, prevents the scarring which so frequently removes all possibility of functional return. Therefore, even in the lumbar area, there may be little place for closed manipulation. Some form of skull traction should be used in every patient with cervical spine injury. On rare occasions this may constitute sufficient therapy but only in the rare case of concussion of the cord. Most often the traction should serve as a prelude to emergency surgery. Any measures short of definitive surgery of traumatized tissue must be considered archaic by present standards. The limiting consideration must be whether harm will result to the patient. With skull traction in place, the patient can be turned in one piece in a turning frame.

It is important that the patient be turned every two hours in order to preserve the continuity of the skin. This can best be accomplished by the utilization of one of the turning frames presently available. Ileus and gastric distention can embarrass respirations and should be treated by intubation.

The ultimate rehabilitation and return of these patients into the community as contributing members of society is dependent on extensive teamwork by specialists in various fields. Consequently, it is essential that assistance from these sources be obtained at the earliest possible moment. There are now many facilities available (but not nearly enough) for this concentrated and cooperative type of care so that there is little need for these patients to be retained in hospitals not equipped for this purpose. As more people with severe disability present themselves for proper care, provisions must be made to meet the demand.

1. Freeman, L. W.: Treatment of Paraplegia Resulting from Trauma to Spinal Cord, J. A. M. A. **140**:949-958 (July 16) 1949; **140**: 1015-1022 (July 23) 1949; correction **141**:275 (Sept. 24) 1949.
2. Freeman, L. W.: Symposium on Neurological Surgery: Injuries of Spinal Cord, S. Clin. North America **34**:1131-1146 (Aug.) 1954.
3. Poppen, J. L., and Hurxthal, L. M.: Normal Cerebrospinal Fluid Dynamics in Spinal Cord Tumor Suspects, J. A. M. A. **103**:391-393 (Aug. 11) 1934.
4. Freeman, L. W.: Observations on Spinal Nerve Root Transplantation in Male Guinea Baboon, Ann. Surg. **136**:206-210 (Aug.) 1952.

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ORGANIZATION SECTION

CONFERENCES ON AGING

The American Medical Association will hold a series of four regional conferences on aging during the autumn months. Sponsored by the A. M. A.'s Committee on Aging and 22 state medical societies, the conferences will be attended by representatives of agriculture, industry, labor, health professions, churches, schools, business, government, women's organizations, communications mediums, and civic organizations.

Dates and locations of the meetings are Sept. 16-17, Hotel Somerset, Boston; Oct. 14-15, Hotel Leamington, Minneapolis; Oct. 28-29, Hotel Cleveland, Cleveland; and Nov. 16-17, Hotel Muehlbach, Kansas City, Mo. In announcing plans for the conferences, Dr. Frederick C. Swartz, Lansing, Mich., said, "We need to explore the opportunities for positive health and meaningful living among older people through exercise of individual, group, and community initiative. With 9% of the nation's population now over 65 and the percentage increasing, it is important for every American to give thoughtful consideration to the aging process and its implications."

According to Dr. Swartz, who is chairman of the Committee on Aging, specific objectives of the conferences are (1) to appraise the significance of the longer life span and its impact on individuals and society, (2) to analyze relationships between social, economic, psychological, and physiological factors and the health of older persons, (3) to explore the opportunities and needs created by a growing population of older persons, and (4) to assess responsibilities of the individual person and of both medical and nonmedical groups in dynamic approaches to the new era of aging.

The Maine, Vermont, New Hampshire, Rhode Island, Connecticut, New York, and Massachusetts medical societies will co-sponsor the Boston meeting. State societies participating in the Minneapolis conference are Iowa, Wisconsin, North Dakota, South Dakota, and Minnesota. The Cleveland conference will be co-sponsored by societies in Ohio,

Michigan, Indiana, Pennsylvania, and Kentucky. Medical societies from Missouri, Kansas, Oklahoma, Illinois, and Nebraska will be hosts for the Kansas City meeting.

PRESIDENT McKINLEY ADDRESSED THE A. M. A.

Dr. Angus L. Cameron of Minot, N. D., has called attention to the fact that President William McKinley briefly addressed the General Session of the Annual Meeting of the American Medical Association in Philadelphia, June 2, 1897. The following account appeared in THE JOURNAL, June 12, 1897, page 1143:

> At this juncture President Senn rapped for order and announced that President McKinley had arrived.
>
> A moment or two later President McKinley came in arm in arm with Dr. Senn, who had returned to the rear of the stage to perform the office of escort, immediately after quieting down the Association. Dr. Hare preceded Dr. Senn and President McKinley; Mayor Warwick and Governor Hastings and Dr. Pepper and the others of the party attending President McKinley, came after. The Association rose and cheered heartily for a minute or two. Quiet being restored, Dr. Senn presented President McKinley, who addressed the Association as follows:
>
> **Remarks by President McKinley**
>
> "Mr. President, Ladies and Gentlemen: Although summoned to this city for another purpose, I deem myself most fortunate to find this honorable Association in its semi-centennial meeting on the same day, and I can not refrain from taking a moment from the busy program mapped out for me by Dr. Pepper, whose assurance I had before coming here that it should be a day of rest. I can not refrain from pausing a moment that I might come into this brilliant presence to meet the learned gentlemen here assembled, and to pay my respectful homage to the noble profession which you so worthily represent. You have my best wishes, and I am sure the best wishes of our countrymen, for the highest results of your profession, and my warm and hearty congratulations upon this, your fiftieth anniversary."

Thus, three presidents of the United States —McKinley, Coolidge, and Eisenhower—have addressed annual meetings of the American Medical Association.

ADDITIONS TO FIELD STAFF

The Council on Medical Education and Hospitals has added three physicians to the staff as field representatives. Dr. Winchell McK. Craig is emeritus professor of neurology at the Mayo Foundation Graduate School of Medicine and a diplomate of the American Board of Surgery, American Board of Psychiatry and Neurology, and the American Board of Neurological Surgery. Dr. George H. Miller from 1944 to 1952 was director of education and from 1952 to 1958 assistant director of the American College of Surgeons. He is a diplomate of the American Board of Internal Medicine. Dr. William W. Fellows became assistant chief medical director for planning in the Veterans Administration Central Office in 1955. He is a diplomate of the American Board of Surgery.

DR. STORMONT LEAVES A. M. A.

Dr. Robert T. Stormont, who has a Ph.D. degree in pharmacology as well as an M.D. degree, left the A. M. A. in August. He was director of the A. M. A. department of Therapy and Research and chairman of its advertising committee. He has been with the A. M. A. since 1950. He leaves to become a vice-president of the Vic Chemical Company, and will take up his new duties on or about Oct. 1.

GOVERNMENT SERVICES

NAVY

Three New Admirals.—Capt. James L. Holland, who is assigned on the staff of the commander, Naval Air, Pacific; Capt. Cecil L. Andrews, commanding officer of the U. S. Naval Hospital, St. Albans, N. Y.; and Capt. Cecil D. Riggs, commanding officer of the U. S. Naval Hospital, Chelsea, Mass., were selected for promotion to the rank of rear admiral in July. They will receive their appointments to flag rank as vacancies occur.

Personal.—Capt. Ralph D. Berry, M. C., was named representative of the office of the assistant secretary of defense (health and medical) and as the Navy medical department representative to the Second Brazilian Congress on Military Medicine to be held in Port Alegre, Brazil, in August. Captain Berry is presently assigned in the U. S. mission to Brazil, Rio de Janeiro.—Capt. M. H. Goodwin, M. C., recently reported to the bureau of medicine and surgery for duty as deputy director, aviation medicine operations division. Prior to this assignment, Captain Goodwin was assigned at the Naval Air Station, Quonset Point, R. I.

NATIONAL SCIENCE FOUNDATION

Scientific Research Program.—The National Science Foundation is continuing its support of the following programs during the summer of 1960 and the academic year 1960-1961: (1) undergraduate research participation; (2) research participation for teacher training; and (3) science training for secondary school students. Colleges, universities, and other educational institutions desiring to consider participation in these programs may receive full information by addressing: Special Projects in Science Education, Scientific Personnel and Education, Washington 25, D. C.

DEPARTMENT OF HEALTH EDUCATION

The papers and introductory remarks that follow were presented at the first Pre-Convention Session on School Health at Atlantic City, N. J., June 7, 1959. The meeting was sponsored jointly by the American School Health Association and the Department of Health Education of the A. M. A.

WELCOME FROM THE IMMEDIATE PAST-PRESIDENT OF THE A. S. H. A.

Ruth H. Weaver, M.D., M.P.H., Philadelphia

The American School Health Association has had very close association with the American Medical Association for a long time. As far back as 1911, a Joint Committee on Health Problems in Education of the National Education Association and the A. M. A. was created to increase interest in the school health program. That same year the Department of Health Education was organized in the A. M. A., and a significant part of the work of the Department has been in the field of school health. The most extensive of the school health activities of the A. M. A. was the creation of the fitness division in the Department of Health Education in 1946, to be concerned chiefly with such problems and employment of a professional consultation staff consisting of a physician and an educator. Today this staff includes W. W. Bauer, M.D., William Bolton, M.D., Fred V. Hein, Ph.D., Donald A. Dukelow, M.D., and Wallace Ann Wesley, Hs.D.

Since 1947 the Department of Health Education has conducted biennial National Conferences on Physicians and Schools at Highland Park, Ill. Members of the A. S. H. A. have taken an active part in these conferences and in helping to interpret school health procedures and encouraging improved professional training in school health of teachers, physicians, and nurses.

Originally the A. S. H. A. was composed of a group of school physicians only. The nurses had their own organization, and the health educators theirs. Today, however, all disciplines have banded together and are working jointly for the good of the school child. Others have joined, including dentists and oral hygienists, and a few—but not nearly enough—school administrators. Health is basic to adequate education; therefore, administrators should be encouraged to participate more fully in school health programs.

The A. S. H. A. now has some 7,000 members, and its activities are carried on by enthusiastic committees. The association is interested in all types of programs concerned with the health of the school child, including immunization, tuberculin testing, communicable disease prevention and control, fitness, safety, and mental health—to mention only a few. Schools throughout the United States rely on advice and recommendations from the A. S. H. A. The pamphlet "Suggested School Health Policies," which the A. S. H. A. helped to revise, is used as a guide in many school systems.

The school physician today acts as an advisor and consultant on health matters, rather than as a substitute for the family physician. He is a liaison person interpreting school health policies and procedures to practicing physicians and interpreting the viewpoint of practitioners to the school personnel. There should be more sharing of school health problems by means of school health councils and community health councils. Sharing frequently leads to the solution of a problem.

We have a unique opportunity to pool our thoughts about the health of the school child at this first joint session sponsored by the A. S. H. A. and the Department of Health Education of the A. M. A.

Director, Division of Medical Services, Philadelphia Board of Public Education.

WELCOME FROM THE PRESIDENT OF THE A. M. A.

Gunnar Gundersen, M.D., La Crosse, Wis.

It is a pleasure to have this opportunity to welcome you, for the American Medical Association, to this first Pre-Convention Session on School Health. It is hoped that sufficient interest in this event will develop so that it may grow into an annual affair. The physicians of the United States, it seems to me, are demonstrating their desire to play a helpful role in the formulation of school health policies and programs. Thus, it seems fitting and proper that a meeting such as this should be conducted in conjunction with the A. M. A. annual meetings.

Most of you are familiar with the long-term work of the A. M. A.'s joint committee with the National Education Association on health problems in education. The National Conferences on Physicians

and Schools, the seventh of which is to be held this fall, are well known to many of you. Also, you are acquainted with the members of the staff of our Department of Health Education, which implements these activities, and their efforts to be helpful in the work of the American School Health Association. Today's meeting provides an example of such cooperative endeavor.

As President of the A. M. A., I have more than a mild interest in matters of school health. I have a strong personal interest, of course, as a grandfather of 11 children and a citizen of a Wisconsin community. But beyond that I have an over-all interest in terms of the medical profession as a whole. For this reason I am particularly pleased to learn of today's trends in school health, because I am informed that these tend to complement and support the private practice of medicine.

I know, for example, that you are doing everything possible to personalize periodic health examinations of pupils by urging that these checkups be made by the personal physician in the privacy of his own office. I understand, too, that in encouraging parents to have needed corrections done you are stressing the importance of getting the child to his physician promptly while the problem is most amenable to treatment. And, perhaps of greatest interest, I know that you are trying to work yourselves out of business by emphasizing for older students—the soon-to-be-parents—the obligations of the home for continuing health supervision.

Some of you know that the A. M. A. has two major themes for this year which permeate all of its programs. These have to do with the problems of nutrition and of aging. It seems to me there is no better place to make a beginning on each of these problems than in the formative school period. During the school years young people can learn the facts and principles of good nutrition and be encouraged to put these into practice. Likewise, they can be equipped with a fund of knowledge and schooled in health behavior that will help to prevent the chronic diseases and to postpone the degenerative processes of aging. This is a mission which could challenge both your personal ingenuity and your professional skills.

From the program I notice that many of the disciplines involved in school health are represented here—educators, nurses, dentists, physicians, and others. I take this opportunity to welcome all of you to this meeting in behalf of the A. M. A. and to wish you well in your endeavors here.

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THE FUTURE OF SCHOOL NURSING

Dorothy C. Tipple, R.N., Albany, N. Y.

It is challenging to have the opportunity to project what the coming years may hold for a profession which has witnessed dramatic changes in the past half-century and which, we have no reason to doubt, will continue to change just as dramatically in the immediate future. It can, however, be dangerous to attempt to predict what the future will bring. We must take care not to impede potential developments in school health service practices by any time-restricted or biased point of view.

The role of the nurse in the school is interrelated with the development and philosophy of school health services. We cannot talk about school nursing as an entity, but only in its proper perspective to the entire school health program. Nor can we look to the tomorrow of school nursing without looking first to its yesterday and today. In the words of Kahlil Gibran's prophet: "Yesterday is but today's memory and tomorrow is today's dream."

It is difficult to achieve a reasonable blending of the practical and the ideal in discussing the future of school nursing. My self-imposed limitation consists of asking, and attempting to answer, four simple questions: 1. Where have we been in school health? 2. Where are we now? 3. Where are we going? 4. How are we going to get there?

Associate in School Nursing, New York State Education Department.

Where Have We Been?

The half-century 1800-1850 marked the early recognition of school health problems primarily in the attempt to detect communicable disease and in efforts to promote more sanitary school living conditions. From 1850 to 1900 we saw progress in control of communicable disease and the first glimmers of the role of the school in health education. From these modest beginnings we have witnessed a veritable mushrooming of activity. We have passed through the strictly preventive phase of school health service and have entered the era of health promotion through education. Today the school health program is one of the most comprehensive services in the school and is generally recognized as an integral part of the total educational program.

Where Are We Now?

As our school health programs have broadened, our philosophy of the functions of the school has been clarified and strengthened. We have recognized that the parents have the primary responsibility for the health and welfare of their children. The school is but one of several community agencies concerned with the health of children and adults. All community services are intended to extend and supplement family responsibility rather than to serve as substitutes.

The uniqueness of the school health service lies in its emphasis on education. The primary function of the school, as one of the official agencies of the community, is education in all its aspects. The health obligations of the school, then, are based on the following responsibilities: (1) to help every child attain the highest state of physical, mental, social, and emotional health of which he is capable; (2) to help every child avail himself fully of his opportunities for education; and (3) to utilize the educational facilities of the school to promote the development of sound health attitudes, practices, and knowledge to enable boys and girls to become increasingly self-reliant in matters pertaining to personal and community health.

Within this framework we recognize the responsibility of the school to establish services to assure adequate health appraisal and health counseling; to make provision for emergency care for illness or injuries occurring at school; to maintain a healthful physical and emotional climate for learning; to make provision for a broad, sequential program of health education; to provide the necessary modifications of program to meet the needs of exceptional children; and to organize programs of in-service health education as necessary for all school personnel.

Obviously every person employed in the school can make a specific contribution to the fulfillment of these obligations. It requires a unified effort on the part of all school personnel to achieve the established health objectives. The school nurse, as a health specialist, has a distinct service to perform. Her contribution has been ably described by Marie Swanson [1]: "The uniqueness of her services lies not in what she does but how she does it." She continues:

> There is no function which is hers alone; she carries no responsibility in which others do not share. Superintendent and principal share her function as liaison between school and home and between school and community. Every teacher, principal, and parent share with her the responsibility for health guidance. Each school employee—administrator, teacher, and member of the maintenance staff—shares responsibility for safe and hygienic conditions in the building and on the grounds. The nurse's value to the school children and to the school organization is in direct proportion to her ability to bring to each of these activities a particularized understanding, scientific knowledge, skill, and effectiveness which is pointedly different from that of other school officers and of parents.

We find a wide range of nursing services being offered in schools today. In general, we can say that most school nurses (1) assist, carry out, or supervise various appraisal procedures to determine the health status of children; (2) maintain an intensive program of follow-through, which includes health counseling with parents and students, interpretation of appraisal findings and health needs to other school personnel, assistance in planning necessary modifications of program, and cooperation with other community health and welfare agencies; (3) help in planning acceptable policies and procedures for emergency care and provide professional nursing judgment and care in case of serious emergencies; (4) assist in educational aspects of communicable disease control; and (5) assist in identification of and planning services for handicapped children. In addition, the school nurse serves as a health consultant to the administrator on all school health problems and assists the classroom teacher as a consultant or a resource person in the program of health and safety instruction.

According to the 1957 census of public health nurses, we have approximately nine and a half thousand nurses employed on a full-time basis by boards of education and many others, employed by voluntary or official agencies, who work part time in schools.

Where Are We Going?

I have attempted to give you a brief overview of our current status—the responsibility of the school, the extent of our present school health programs, and the role of the school nurse. Now, where are we going from here? On the basis of the past century of development, there are several factors we can safely assume. The first one is that the public will continue to expect more of nursing service in general and of school nursing service in particular. A committee of the National League for Nursing recently issued a statement entitled "What People Can Expect of Modern Nursing Service." Two of the basic assumptions indicate the trend toward comprehensive nursing service: 1. "Nursing care encompasses health promotion, the care and prevention of disease or disability, and rehabilitation, and involves teaching, counseling and emotional support as well as the care of illness." 2. "Nursing care is an integral part of total health care and is planned and administered in combination with related medical, educational, and welfare services."

Second, educational programs today and in the future are, and must be, influenced by socioeconomic changes in society. For example, trends in population growth and distribution, with their effect on family living, are factors to be considered in planning for desirable mental, emotional, and social aspects of child development.

And, third, health needs of children change with the socioeconomic advances of society, with progress in medical knowledge, and with increased understanding of child growth and development. School health services in the future must be based on priorities established by an impartial study of these changing needs. For example, since accidents are the leading cause of death of the school-age child, we see clearly the need for intensive safety education. With the present focus on prevention of juvenile delinquency, we see the school's responsibility to cooperate with parents and with other

youth agencies in the development of an environment more conducive to social and emotional adjustment.

An awareness of these, and other factors, makes it possible to predict, with some degree of assurance, areas in which school health services should continue to expand. We will broaden the base for appraisal activities, with less emphasis perhaps on their value as case-finding procedures and more emphasis on their educational value. The school nurse will devote a greater percentage of her time to health counseling activities with students, parents, and school personnel. She will increase her services as a consultant in school health problems to the administrative staff. There will be a much closer correlation between health services and health education. We will see the school nurse making a much more specific contribution to the development and implementation of the health education curriculum. We will see the nurse carrying increased responsibility for mental, social, and emotional aspects of the health of children and school personnel. We will see a more unified approach to the complex problems of children through effective coordination of special school services. We will see the nurse carrying major responsibility for planning and effecting programs of in-service health education for school personnel. We will have more effective coordination of specialized school health services with the health and welfare services in the community.

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How Are We Going to Get There?

So far we may safely go in looking ahead, for these paths are already marked. There is nothing startlingly new. There are questions of priorities in program planning and there are problems related to understanding, development of standards, and professional leadership. Our real concern is not where we are going, but how we can move effectively from where we are to the place where we must be to provide the essential services to meet the needs of youth.

First, we need to develop an understanding on the part of an economy-minded public of the long-range values coming from a program such as has been outlined. Statisticians have arrived at figures to explain costs of medical and hospital service. There are figures to demonstrate the value returned, in terms of money and service, of the cost of rehabilitation. Who can measure the economy not only of prevention but of positive health? Who can place a monetary value on the worth to himself, to his family, and to society of the person who is operating at his peak of efficiency from the standpoint of physical, mental, social, and emotional health? We have never utilized fully the potential resources of the school to demonstrate the economy of positive health. This must be one of our goals.

Second, we must develop programs of nursing education to provide the expertness needed to carry out the specialized services in the schools. We are currently looking at our nursing education programs to determine how effectively they provide this expertness and whether they provide it to the degree required. If additional preparation is needed, where shall it be given—as part of the baccalaureate program or on the graduate level? The American School Health Association and the National League for Nursing, in cooperation with the Children's Bureau, are studying this complex problem. Research and experimentation will be necessary in order to determine the most effective preparation for school nursing.

Many states are currently attempting to set up certification requirements for nurses employed in the schools. The primary purpose of certification is to provide standards of preparation to improve the quality of service. Such standards, to be effective, must be closely aligned to programs of nursing education.

In addition to the work of the Children's Bureau, the National League for Nursing, and the A. S. H. A., the American Nurses Association has been engaged in preparation of a statement of the function of school nurses, as well as recommended standards for certification. Thus we see nursing leadership emerging on a state and national level to come to grips with this fundamental problem of professional preparation for school nursing. It is perhaps the single most significant aspect of the sincere attempt to extend and expand school nursing service by well-qualified and competent persons.

No professional group has made a greater effort to gear its service to the needs of mankind than has the nursing profession. There is every indication that school nurses will continue to evaluate existing services and will have enough of the pioneer spirit to meet the demands of the continual and rapid change which is characteristic of our society.

Comment

My remarks have been predicated on the assumption that we must take an unbiased, long-term view of school health programs and build soundly and wisely for the future. On the other hand, we must face the urgency of our situation. The future may be 20 years ahead, but it is also upon us now. It is immediate, and we cannot face its challenges with complacency. The outcome of good school health programs may well constitute an essential component of the world-wide struggle for peace and survival. This concept has been succinctly stated by Elmo Roper [2]: "The real pulse of our civilization is human lives, lived in freedom and dignity, by men who are conscious of their own

stature and deeply respectful of the human potential that all men possess. We will be saved—if we are lucky—by men who are able to use all that is in them—their minds, their senses, and their hearts—as fully developed human beings."

We in school health work have an increasingly vital role to play in the maximum development of men and women capable of functioning effectively in our society. We must bring to this role an intense and an intensive conviction of the true worth of this service to the children and youth of America.

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MODERN APPROACHES TO SCHOOL DENTAL HEALTH PROGRAMS

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To understand present concepts of modern dental health and their importance in any program for the prevention, control, and treatment of dental diseases, one should ask, "Do I want to go through life with healthy teeth and healthy oral tissues?" Of course all of us want lifetime teeth and healthy mouth tissues for complete health, happiness, comfort, aesthetics, and social acceptance. This positive response, indicating that dental health is an integral part of total health, is based on an awareness, an attitudinal behavior, and a willingness to accept certain responsibilities relating to health principles.

Responsibilities Relating to Health Principles

The first of these is the responsibility of gaining dental health knowledge concerning the general mouth structures and functions and the general causes, manifestations, and sequelae of dental disorders in relation to other organs of the body. The second responsibility is the initiation of regular daily adequate personal home care—oral hygiene. The third responsibility is concerned with obtaining routine periodic examination, preventive control measures, and maintenance care by the attending dentist.

This awareness of, and interest in, oral health coupled with a cooperative point of view on the part of the health-minded patient will greatly diminish the amount of remedial care needed and reflect in reduced dental expenses, elimination of pain, fewer lost teeth, less discomfort, less time loss and absence from school or office, and fewer days of indisposition and ill health.

The fourth responsibility is to effect a proper daily, balanced, nutritional diet, emphasizing a low intake of sugar-rich foods. The fifth responsibility concerns community acceptance of the procedure and action to provide potable fluoridated water (1 ppm) to increase the resistance to decay of tooth structures, internally and externally. Fluoridation is the most effective, safe, efficient, and economical preventive measure in dental public health, accounting for a reduction of 65% of dental decay in children. The greatest hope for a realistic solution to the widespread problem of dental caries is in the consumption of fluoridated water, because of its easy application for large numbers of people and its relatively low cost. Consumption of fluoridated water should start with the pregnant mother for greatest anticariogenic effectiveness in the newborn infant. Goethe, the German poet, has said: "Little can be accomplished for grown-up people, the intelligent man begins with the child."

From the Department of Public Health.

Extent of Dental Disease

What is the extent of dental disease? Tooth decay is man's most common disease, attacking 95% of our population. Dental caries is the greatest cause for the loss of teeth during childhood and adolescence, and it accumulates many times faster than it is corrected. Gum diseases and diseases of the supporting tissues of the teeth are mainly responsible for the loss of teeth in later years. Oral diseases, malformations, malocclusion, cleft palate, and cleft lip contribute to many physical, mental, and emotional health problems, including speech defects, personal appearance, and social adjustment.

Fifty per cent of all 2-year-old children have one or more decayed teeth; 80% of 6-year-old children have decay in deciduous teeth. At school age they have an average of three or more deciduous teeth attacked by dental caries, with 14% having decay in their newly erupted first permanent (six-year) molars. The average 16-year-old has seven or more decayed, missing, or filled teeth involving 14 tooth surfaces. In any given age group 30% of children require orthodontic treatment, and it is probable that today's children will lose 50% of their teeth before the age of 40 years.

These statistics reveal the presence of a universal public health problem, according to the conditions of the definition of Dr. N. Sinai, of the University of Michigan, who says, "A public health problem is: 1. A condition or situation which is widespread, and an actual or potential cause of morbidity or mortality. 2. About this situation, there is a body of knowledge which if applied, would prevent, ameliorate or cure this condition or situation. 3. This body of knowledge is not being applied."

We have today the dental problem of a tremendous backlog of unmet dental needs, which is increasing greatly each year. It is estimated that in the United States there are 300 million cavities in the teeth of school children, and that there will be an increase of 40 million cavities per year under present methods of dental health care. However, it is possible to solve this problem with a long-range plan of community attack through a total community project. To attain success, the people of our communities as a group must participate and come to know the truths about the control of dental diseases.

Responsibilities of Dentist

At all levels—individual, family, community, state, and nation—the dentist has direct responsibility for implementing dental health. He has this responsibility as a citizen and as a member of the dental profession. His responsibility as a citizen parallels that of other citizens; his responsibility as a member of the dental profession is to keep himself informed of scientific advancement and to provide complete high-quality dental services to his patients. As a member of his dental society, he should assist in developing plans and policies to guide community agencies and institutions in the development and maintenance of health services as these relate to dentistry. He serves through his dental society as a connecting link between official and voluntary organizations that have the authority and resources to make the professional policy work effectively in the interest of the public. Thus, dentistry makes an important contribution to community health.

Objectives and Financing of Programs

The long-range objectives of a community dental health program should include comprehensive dental health education and periodic preventive, control, and corrective measures to the end that every person in the community may have available the preventive knowledge and dental care that will assure him a comfortable and healthy dental condition. The last objective is evaluation and research—a determination of baseline data, concerned with the efficiency, the progress, and the effectiveness of the program and the minimizing of the need for remedial dental services.

The financing of dental health programs is the responsibility of the community. I am in accord with the American Dental Association principles that the individual should take care of his own needs. When this is not possible economically, it should become the responsibility of the community, and then of the state. When community school programs for dental health are developed and established, it is the responsibility of the community or the state, as the case may be, to provide for the financing of such programs. The duty of the profession is to see that the dental program is administered according to the best procedures involving good professional and scientific services.

Progress in Dental Health Programs

As I see the picture in New Jersey, we are proudly making progress in school dental health programs in our communities because of greater coordination, cooperation, consultation, and participation with the official and voluntary institutions and agencies interested in health activities. Our two new colleges of dentistry (Fairleigh-Dickinson University and Seton Hall University) and Rutgers University during the past four years have sponsored conferences on dental health and dental health education. The New Jersey state departments of health, state department of education, Congress of Parents and Teachers, New Jersey Education Association, New Jersey Health Officers Association, the Medical Society of New Jersey, and the New Jersey State Dental Society are some of the organizations that are cooperating in dental health activities.

More dentists are cooperating in rendering preventive and maintenance care of children in our school dental programs. More chairside dental health education is imparted, emphasizing home care and evaluation of dietary requirements. More children are receiving dental health instruction through school dental inspections by dentists; as a result, they are motivated to seek adequate dental care. There is a slight increase in the number of dental hygienists employed by our schools. More communities are fluoridating their water supplies. Topical applications of 2% sodium fluoride are routinely utilized for clinic patients at ages 3, 7, 10, and 13 years in areas with nonfluoridated water.

Future Goals

Much remains to be done to influence direction and action of our community school programs for optimum dental health:

1. Fluoridation of our community drinking water to decrease decay by at least 60 to 65%.

2. Adoption of voluntary prepayment and postpayment plans to aid indigent children and those with borderline incomes and their families to pay for dental care.

3. Creation of a dental health section, bureau, or division in the local department of health and board of education of every community, adequately staffed with dental consultants trained in dental public health and health education.

4. Setting up of adequate and expanded dental facilities, geographically distributed, preferably located in health centers and schools.

5. Development of increased dental man power—well-trained, kind, industrious, dedicated, adequately compensated school and health department dentists, dental hygienists, dental assistants, and

clerks—for successful operation of a community's dental health services in coping with the backlog of unmet dental needs.

6. Giving of systematic, regular, and interesting dental health instruction as an integral part of every school curriculum at every age level. (In some states, dental hygienists are licensed to teach dental health. The state of New Jersey is considering the recognition of the school dental health teaching ability of the hygienist by adopting necessary legislation.)

7. Making of school surveys, inspections, and examinations, conducted twice a year by a dentist and not by a physician, nurse, or teacher. This is the dentist's responsibility in his own professional field. (Unless it is possible to institute a definite follow-up program to assure that needed dental corrections are being made, or to find out the reasons for lack of care, the value of a dental inspection and examination program is questionable. Without these it is a waste of time, money, and personnel.)

8. Giving of education in schools on the sale and consumption of confections, soft drinks, and other foods containing objectionable, readily fermentable carbohydrates.

9. Devising of an eligibility formula for dentally indigent admissions to clinics, by the school nurse or other authorized personnel, with the advice and approval of the local dental society and the area dental health committee.

10. Provision of clinic programs continuous throughout the entire year, with dental health education and dental service personnel stressing the fact that "dental caries do not take a vacation."

11. Provision of special dental services for preschool and physical and mentally handicapped children.

12. Encouragement of older school children to enroll in science clubs and in school health clubs, with special attention to the study of dental health and participation in community health and science fairs. (Vocational guidance of prospective students in dentistry and its auxiliary branches should be encouraged through consultations with the local dental society.)

13. Release of children by school authorities to keep dental appointments during school hours, to maintain optimal clinic service efficiency and capacity load in rendering chairside dental care.

14. Inclusion of dental health as a dynamic integral part of Parent-Teacher Association activity in every school, with every community having a community dental health council vitally interested in program study, research, evaluation, and the development of methods for solving the complex problem of dental disease.

In the broadening of programs that have not been rendering complete service for the entire school-age indigent group, and in establishing new programs, an effort should be made to gradually develop complete service. This can be accomplished by inaugurating a program that starts with the provision of complete service for the lower age group and then gradually is expanded, grade by grade, until all are receiving complete service. Until all are being serviced, only emergency treatment can be rendered for grades not in the complete program.

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TRENDS IN SCHOOL HEALTH INSTRUCTION

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It was Lemuel Shattuck who, in presenting the report of the Sanitary Commission of Massachusetts, in 1850, fathered the idea that American schools should instruct all children and youth in matters relating to health and hygiene. Not until 1918, however, did the idea receive the official stamp of approval that schools do, indeed, have a responsibility for the health and health education of the child. At this time the Commission on the Reorganization of Secondary Education recognized health, including health education, as one of seven major objectives to guide secondary education in American public schools. Originally described as the seven cardinal principles of American secondary education, these objectives were immediately recognized as ones which might well guide all American public education. So they became, and so they remain.

It is of significance, as one views these and subsequent developments in retrospect, that 1918 was little more than 40 years ago. Those experienced in public education know that a lag period of 20 to 30 years, between innovation and implementation throughout the general structure of public education, is par for the course; that departure from tradition is seldom rapid. Wholly consistent with this fact has been the failure of more than a few schools to implement, in fact, truly meaningful programs of health instruction. There are barren areas in health instruction, areas which give lip service to it while denying the same in quantity and quality. There is need for changed thinking on the part of some who, while condoning the incursion of every imaginable subject, and some which defy the imagination, deny a place in the same curriculum for instruction in an area of learning which is as essential to successful living as is instruction in the language which makes learning and communication possible. There is need for careful curriculum planning of a kind which will assure health instruction for every pupil in every American school. There is need for teaching methods which will narrow the gap between knowledge

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of the facts of health and the principles of healthful living, and the actual practice of healthful living.

The aforementioned facts have been presented only for the purpose of emphasizing the significance of those which follow. These are in severe contrast. They afford clear-cut evidence of progress to gladden the hearts of all concerned with health and health education and, specifically, health instruction. They evidence diligent and persistent efforts on the part of educators and health workers alike. They suggest the "coming of age" of health instruction.

Joint Efforts

Perhaps the clearest, and possibly the most significant, of the trends which currently reflect progress in health instruction is that of joint effort on the part of educators and health personnel to evaluate existing programs, to suggest their improvement where indicated, and to assist school personnel in implementing the new or improved activity. Part and parcel of an interest in the total school health program, to be sure, this action continues to develop on many fronts, much to the advantage of health instruction.

Numerous agencies and organizations which, for want of space, may not be mentioned here, have participated in and continue to contribute to this effort. Their devotion of time, effort, skill, and even financial aid has brought interdisciplinary action which has resulted in improved understanding of needs, objectives, and responsibilities in this area of school work.

This trend continues and is seen at its best in the biennial Conferences on Physicians and Schools sponsored and conducted by the American Medical Association. These thoroughly professional working conferences and their counterparts on the state level continue to focus a penetrating light on the needs of school health, including health instruction. To the extent that they will continue to be influential in the improvement of health instruction programs, they will perpetuate a trend the important significance of which must be clear to all.

Similar to the foregoing, organized in the same spirit, and very much a part of the same trend are the school health councils now frequently seen at both local and state levels. To the extent that these groups are, or will be, favored by school cooperation which reflects desire for and sincere intention to implement needed improvements, their contributions to health instruction must inevitably prove invaluable.

Preparation for Health Instruction

A second clearly apparent trend, one noted in all sections of the country, is that toward increased and improved preparation for health instruction of teachers at all school levels. It is indicated especially in the numerous school health or health curriculum workshops which are now offered during summer periods and as intensive, short-term operations during the school year; by increased enrollments in evening college and extension division programs; and by completely local, in-service training courses developed within local school districts. Undergraduate preparation of elementary classroom teachers also appears to be placing added stress on quality of content, more artistic use of method, and the use of a variety of selected teaching aids and materials.

The great advantage of health curriculum workshops, institutes, and other in-service studies is found in the opportunity for the teacher to relate such studies to peculiarly local social and health conditions, to the needs of the particular age group which he serves, and to keep abreast of, for example, the newer knowledge of nutrition; changing community, public, and world health conditions; and advances in medical science which have implications for health education.

This trend has been greatly enhanced by the interest and support of the voluntary health agencies, which have seen the advantage of preparation for healthful living at the stage in life when attitudes relative to personal and public health are forming. The conclusion that children will be best prepared for healthful living when the teacher is well qualified to teach is inescapable.

Literature and Teaching Aids

The plethora of good textbooks, of supplementary health education literature, and of new and improved teaching aids which has become available in recent years suggests another trend of no small importance. This is the trend away from dependence on "home-brewed" and limited materials of instruction to one of demand for instructional aids and materials of superior quality which recognize the factors of motivation, attitudes, and age-group interests, needs, and behavior. With few exceptions the postwar years have been good-vintage years in this respect.

Textbooks prepared in series for use in grades 1 through 6, or 1 through 8, now facilitate a desirable, progressive continuity of instruction while precluding the stifling duplication and repetition which typified the "spinach and toothbrushing era." Simultaneously, they stimulate interest and desire to read on the part of the pupil and reduce the burden of the classroom teacher who is not a health specialist. Likewise, new books have been prepared for use in grades 7 through 12. These, too, are now of im-

proved, even exceptional, quality and, like their lower-grade counterparts, tend more and more to assure scientific accuracy, psychological soundness, desirable degrees of concreteness and abstraction, and appropriateness (considered in terms of vocabulary, sentence structure, reading ability, and reading comprehension) to the materials of health instruction.

Supplementary reading materials which are free or available at small cost, many of which were once suspect, likewise now provide a rich fund of material for use in school classrooms. These materials not only extend the coverage of health topics and the reading range of pupils and students but increase the health knowledge of teachers and are invaluable to schools which are denied a proper armamentarium of standard teaching materials.

This demand for and use of high-quality teaching aids and materials is now a well-established trend, one which has brought an added degree of stability, and an added inducement, to health instruction at all grade levels.

Objectivity of Measurement of Learning

Another meaningful trend is that toward increased objectivity in the measurement and evaluation of learning. This trend, although apparent, remains to be clearly defined. However, the idea that a subject worth teaching is worthy of measurement and evaluation has been recognized in health instruction, and standardized tests and scales of health knowledge, of health knowledge application, and of attitudes are being used with increased frequency in support of teacher-prepared tests and subjective appraisal procedures. There is evidence to indicate that when, in teacher preparation, and especially in in-service preparation, teachers are familiarized with available testing materials and the possibilities for their use, this knowledge finds ready application in the classroom.

Quite obviously, this trend will be accelerated as newer and better tests are devised, as time allocations for health instruction are increased, and as teacher preparation for health education places added stress on the need for and importance of objectivity in measurement and evaluation in health instruction.

Time allocations for health education in elementary and high schools have long since been proposed by the most interested and responsible groups in education and health. As proposed, the recommendations suggest for the elementary grades an amount of time at least equivalent to that devoted to other major studies and for the secondary grades (7 through 12) a minimum of one period of instruction daily for two semesters during the period grades 7 through 9 and a similar amount during the years 10 through 12. In addition to time allocations, the plea has long since been made for the provision of this instruction in secondary grades by teachers especially qualified and certified for such teaching in the stead of instruction given by teachers in related or other areas of instruction.

Despite these recommendations, a paucity of evidence is available which would indicate general acceptance and compliance with them. It is, then, especially gratifying to note a trend in secondary schools toward increased time allocations as well as toward the assignment of these responsibilities to specially trained or qualified teachers. While this is by no means general, it is wholly consistent with the general pattern of progress in American public education, a pattern which indicates that innovation or change tends to be initiated locally or sectionally and only gradually to seep into and gain acceptance in other areas to the point of becoming general practice.

Regrettably, no similar increase in time allocations in the elementary grades is noted at this time. Extreme differences in time allocations have typified, and remain typical of, health instruction at this level.

Social Nature of Health

A trend, much needed and long delayed, is now apparent. This is toward strengthening instructional efforts in behalf of understanding of the social and environmental aspects of health. While health instruction originated as a study of the basic facts of physiology and the influences of alcohol, and was so limited for many years, it is tending more and more to give recognition and desirable emphasis to the social nature of health and the social and environmental influences in health and disease. This recognition of the concept of an epidemiology of health, even as we stand on the brink of a space age, is one trend the significance of which needs little elaboration.

Comment

These, then, are the trends in health instruction which appear to be of significance at this time and to foreshadow even more and better instruction in the future. They suggest the metaphor that the patient, in this instance, enjoys a good, if precarious, state of health and that the prognosis is excellent, given a liberal dosage of tender, loving care, coupled with continued efforts to assure a state of abundant health in the future. We of the American School Health Association and the A. M. A. must continue our efforts in behalf of this objective.

CHANGING ROLE OF THE PHYSICIAN SERVING THE SCHOOL

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One might suppose that the role of a school physician is easily changed by a new state law, a revised educational policy, or a recent discovery in medical science. Such is not the case. The school physician, like the medical practitioner and the health educator, responds to scientific and social change in a most gradual manner. This is as it should be. For those who grow impatient at times, I recommend reading a history of public health. It will provide a wonderful perspective for the changes that slowly occur for school physicians and school health practices.

It is for just over 50 years that physicians have been serving the schools. They were brought in to exclude children with contagious diseases and to investigate the unsanitary conditions that were so common. There followed a slow recognition that periodic health examinations (annually at first) would contribute to the education of children. This policy was gradually revamped after 1942 as it became clear that health examinations should be more thorough and less frequent; that they should be performed, if possible, by the family physician; that a nurse-sponsored follow-up was necessary; and that teacher-nurse conferences should seek out those children who needed special attention. Remember, in 1942 these were relatively new ideas.

Basic Principles

Today these recommendations have been gradually accepted in most areas. It is my purpose to outline in more detail the changing role of the physician serving the school. However, before outlining these details, it will be helpful to review certain principles that should be kept in mind if the school physician is to carry out his new role:

1. Responsibility for the school child's health rests with the parents. Others may advise and offer help, but the parents are the ones who must carry out their obligations.

2. Health examinations and treatment, if indicated, are the responsibility of the family physician. Where there is no physician available, the examination is performed by the school physician. Referral is then made to a physician of the parent's choice.

3. The school person who can be most helpful in detecting symptoms or abnormal behavior is the classroom teacher. He should be a constant aid in finding those children who may need medical attention.

The school nurse is in a position to give personal health counseling to the child, to his parents, and to his teacher or teachers. The nurse should amplify the role of the physician in addition to her other important duties.

With these principles in mind, the school physician plays a key role as a health specialist and counselor.

1. He encourages parents to have the child examined by the family physician, who reports the findings on appropriate health records.

2. He examines those children who fail to have a private examination.

3. He examines children who are referred by the school nurse, the teacher, and the school counselor. They need this special service to carry out their educational functions intelligently.

4. He evaluates the screening programs done in the schools—visual, auditory, and developmental.

5. He interprets the findings of the health examination to the parents, the child, and the school nurse, and to the teacher as the findings relate to the child's educational capability.

6. He advises the school administrator about certain individual handicaps that may alter the child's educational program.

7. He consults with the family physician when school activities impose a physical or mental burden on a child.

8. He is in the enviable position of coordinator between the private physician and his medical society, and the classroom teacher and his school administrators.

The school physician can furnish the answer to the questions, "How can the educator get from the private physician information about a child's health necessary to this child's educational program?" and, conversely, "How can the educator help the private physician learn what the school is trying to do, and why such information about the child-patient is important?"

Necessary Health Projects

Now that we realize that frequent examinations of healthy school children are not fruitful, we discover a vast amount of professional work that needs to be done. These health projects are usually recognized as necessary by the school administrators, the health professions, and the community (parents) who comprise the school advisory health councils.

Public Health Practices.—Tuberculin testing has received a new impetus because of the low yield from mass chest x-ray surveys and the use of antituberculosis drugs. Communicable diseases and their control are still with us, in spite of new weap-

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ons to combat them and new regulations about them. The normal school-to-home channels of communication helped immeasurably in the recent poliomyelitis immunization programs. Screenings for diabetes, for cystic fibrosis, and for the carriers of the beta-hemolytic streptococcus of rheumatic fever are noteworthy procedures. Recently there have been surveys on physical fitness of school children and on allergies in the schools. The education of school personnel and children themselves in first-aid procedures is in the province of the school physician. The day has come when everyone must know something about simple, basic first-aid and self-aid. All of these are fertile fields for the school physician; no one else can answer these health needs quite so well.

The Handicapped Child.—The school child with a visual or hearing handicap, the orthopedically disabled child, and those with cardiopulmonary disabilities and mental retardation and damage must be educated to the limit of their and our resources. There is an ever-present need for close liaison between the treating physician and the educator. The school physician can interpret the needs of each to the other for the ultimate benefit of the handicapped child. Recently a program on individual remedial physical education has received much favorable attention. We know that good posture is related to good health and well-being. The school physician works closely with the physical education department in this enterprise of remedial exercises.

Mental Health.—No field has received more publicity and less definitive action than the field of mental hygiene. Psychiatrists have appealed to the general practitioner to accept a share of the community load. The load could be lightened by simple measures of the physician who serves the school.

The school physician knows that emotional well-being begins with the self. His emotional well-being reflects on the teacher, the nurse, and the administrator by application of empathic relations. The children in turn can reflect positive attitudes of the physician, the nurse, and the staff even in the face of discouraging environments. The school physician should take time to talk with and listen to the teachers and the children. He can be a major influence for a good emotional climate in the school if he will but practice what he knows about mental health.

Health Education and Counseling.—Individual health counseling is an activity that merits the constant attention of the school physician. In this he works in harmony with the school nurse. When a child comes to the health room for a health examination, he is receptive to health counseling. When the mother accompanies the child being examined, she, too, is receptive to health counseling. When a child is ill and the parent is notified, they are both ready for health counseling.

Health education took a dramatic turn for us in the Philadelphia school district recently. A weekly series on radio station WFLN entitled "The Doctor Says" brought the comments of many outstanding physicians to the children of the upper elementary grades to their parents at home. "Fit as a Fiddle" was a television series of 33 programs beamed to all the schools in the area. Part of the series was on the human body, with emphasis on health and safety practices and on physical fitness. A great deal of interest was shown by the participating schools.

Health protection can move only as fast as public opinion will permit. Health education is our weapon to be used against ignorance and apathy in order to attain this desirable goal.

Methods for Part-time School Physician

The physician who occasionally serves the school in the smaller districts must be selective in his methods. It is not enough to examine the required number of pupils as provided by school health laws. I would suggest five steps for the occasional or part-time school physician to take in order to serve efficiently and helpfully:

1. He should learn the objectives of the school program and how they relate to the health of the child.

2. He should inform the school administrator about his visiting schedule and the nature of his visits.

3. He should spend time with the teachers in order to inform them on how to look for signs of illness and disability.

4. He should be prepared to assist parents in referring a child with a defect to his private physician or a treating agency.

5. He should ask the nurse to select those children to be examined in a priority of importance. This sorting would depend on degrees of communicability and remediability of conditions and on amount of disability. Also, the parents must learn to bear responsibility for the school child's health in smaller school districts to an even greater extent than they do in school systems with highly developed health services.

Comment

I would like to introduce a new term to characterize the changing role of the physician serving the school. We have known for years about the bedside manner of the ideal physician. An objective for the school physician is a "schoolside manner."

This concept assumes that the school physician is professionally trained and active in medical and community affairs. He must have a genuine interest and an orientation in the objectives of the school health program. And then he must carry all of those traits of the ideal physician into the school situation. Without doubt the physician who serves today's school has a complex but a most rewarding task.

MEDICAL NEWS

ARKANSAS

Predict Increase in Use of Water.—Industrial use of water in Arkansas is expected to double in the next 15 years, according to a report on the state's water resources released by the Industrial Research and Extension Center of the University of Arkansas. Agricultural use of water also will double, while domestic use will increase about 85%. The report is a comprehensive study of the availability of surface and ground water in Arkansas, its quality, and its present and future uses. It is estimated that the total use of water for industrial, domestic, and agricultural purposes in 1957 was about 420 billion gallons. This is a daily use of 1,151 million gallons. Eleven per cent of the total was used by industry, 8% for domestic purposes, and 81% for agricultural enterprises. The projected need by 1975 is estimated to be 855 million gallons or 2,342 million gallons daily. This is an increase of 104% in the total water usage, but the percentage of distribution among industrial, domestic, and agricultural uses will be about the same. Despite the increased use of water, it was stated that the state's water supply is "more than ample for generations to come." The primary water supply was 40 times greater than the 1957 usage. By 1975 the supply will be 20% greater than projected usage. Water problems in the future will primarily be those of distribution. Uneven rainfall and inadequate distribution systems have caused shortages in some Arkansas localities. Another problem in some areas is pollution.

DISTRICT OF COLUMBIA

Plan Health Research Facilities.—The Department of Health, Education and Welfare announced a grant of $350,000 to Georgetown University for use toward the construction of health research facilities. The grant is to be matched by the university. The construction made possible by this grant will be part of the Georgetown University Science and Basic Health Research Building. Groundbreaking is scheduled for the spring of 1960. Georgetown's new science building, estimated to cost 3½ million dollars, will provide the basic science research facilities to supplement applied research in the diagnostic and research building recently completed in the Medical Center.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Anesthesiologists Meeting.—The Illinois Society of Anesthesiologists will meet Sept. 20 at the Sheraton Hotel, Chicago. The scientific session, beginning at 9:30 a. m., will include "Current Concepts in the Treatment and Prophylaxis of Shock," by Dr. Thomas H. Selden, Newport News, Va., and "The Legal Aspects of Anesthesiology," by Dr. Carl E. Wasmuth, Cleveland. All members and guests are invited to attend the noon luncheon ($3.80). Dr. Richard E. Lyons, Evanston, is chairman of the program committee. For information, write Miss Margaret I. Maloney, 25 E. Washington St., Room 1224, Chicago 2, Executive Secretary.

Chicago

Prize for Medical Investigation.—The Institute of Medicine of Chicago, 86 E. Randolph St., Chicago 1, is offering a biennial prize of $500 for the best investigation in medicine or in the specialties of medicine. The work may be also in the basic sciences, provided it has a definite bearing on some medical problem. Competition for 1959 is open to graduates of Chicago medical schools who completed their internship or one year of laboratory work within a period of five years prior to Jan. 1, 1959, excluding their terms of service in the Armed Forces. Manuscripts must be submitted to the Secretary of the Institute of Medicine of Chicago not later than Dec. 31. The manuscript of the prize paper is to become the property of the institute. The prize winner may be invited by the board of governors of the institute to present his paper at a meeting of the institute. If no paper submitted is deemed worthy of the prize, the award may be withheld at the discretion of the board of governors.

New Allergy Laboratory.—A new allergy research laboratory was set up in the Research Institute of Michael Reese Medical Center by the department of allergy, Dr. Milton Mosko, department chairman announced. The facility is headed by research associate Peter Baram, Ph.D., who joined the institute staff after three years as microbiologist at Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C. The laboratory was established with a twofold purpose: to carry on basic research in immunity and allergy and to permit residents and staff members in the department to participate in and develop basic science investigation. The laboratory is engaged in investigating the relationship between allergy and immu-

nity. The work of the research laboratory is supported chiefly by the Jessie Werthamer Service Club, which furnishes more than half its operating funds. The new laboratory is housed in the Nelson Morris wing of the Research Institute at 2900 S. Ellis Ave.

KENTUCKY

Antique Collection for Restored Apothecary.—Chas. Pfizer & Co., Inc., through its Pfizer Laboratories and J. B. Roerig & Company Divisions, presented a rare collection of 18th and 19th century pharmacy equipment, glassware, and ceramic jars to the recently restored McDowell Apothecary in Danville. The shrine, honoring Dr. Ephraim McDowell, pioneer surgeon who was the first to perform successfully a major abdominal operation, has been restored by the Kentucky State Medical Association and the Kentucky Pharmaceutical Association. The 180-piece collection was installed in time for the dedication of the apothecary on Aug. 14. The collection includes glassware of striking period design made by early craftsmen in Scotland, England, France, and the United States. Among the older pieces are 12 English Delft drug jars dating back to the middle of the 18th century, two rare green carboy-shaped stock bottles made in Scotland about 1780 and a massive, attractively decorated leech jar. There are also examples of glassware used by the McDowell Apothecary from 1795 to 1856, as well as early American mortars and pestles and balances. Dr. McDowell opened the apothecary in 1795 when he began to practice in Danville. It was the first drug store west of the Allegheny Mountains. The apothecary and the doctor's office in the rear adjoin Dr. McDowell's home which was restored and opened to the public in 1939.

MASSACHUSETTS

Society News.—Elected to office in the Massachusetts School Physicians' Association for the next two years were: Dr. Sidney S. Listernick, of Everett, president; Dr. Jacob Brenner, North Easton, vice-president; Dr. Walter N. Secord, Watertown, secretary-treasurer. The association is celebrating its 10th year with a membership roster of over 200 school physicians.——At the annual meeting of the Massachusetts Society of Anesthesiologists, the following officers were elected: president, Dr. Phillip S. Marcus, Boston; vice-president, Dr. Robert W. Gladstone, Pittsfield; and secretary-treasurer, Dr. John H. Tucci, Brockton.

Combine Obstetrics and Gynecology Departments.—Dr. George P. Berry, Boston, dean of the Faculty of Medicine at Harvard Medical School, announced the joining of the research and teaching activities of two academic departments—obstetrics and gynecology—to form a single department of obstetrics and gynecology. The decision to combine the two departments "to increase the learning opportunities for tomorrow's physicians, professors, and investigators," followed two years of study by a committee of the faculty of medicine at Harvard. Their findings included the proposed reorganization of the departmental structure and of the teaching programs concerned with lectures, seminars, and laboratory sessions. The goal of the department of obstetrics and gynecology, Dr. Berry pointed out, will be "to produce full-time teachers and investigators to meet the rapidly expanding need of this field of medicine." Students specializing in obstetrics and gynecology will be expected to devote a minimum of two years to general surgical training, three years in obstetrics and gynecology, and two years in the basic medical sciences.

Campaign for Building Program.—A November campaign to raise $600,000 among medical alumni for the Boston University Medical School Building Program was announced jointly by President Harold C. Case of the university and Dr. Ronald W. Adams, of Newton Centre, chairman of the alumni campaign committee. The alumni campaign is part of the university's medical development program. Now under construction is Boston University's 3-million-dollar medical school research building, adjacent to the university's present School of Medicine and the Massachusetts Memorial and Boston City Hospital, begun last March. As the first step in the 10-million-dollar long-range development program, this will provide facilities for basic and clinical research by faculty and graduate students. The program also includes 3 million dollars to build a classroom and teaching laboratory building as well as 4 million dollars for endowment for medical education. The committee for fund raising will be headed by Dr. Adams, a graduate of the Medical School in the class of 1933 and an instructor in orthopedic and fracture surgery.

MICHIGAN

Maternity Beds.—Michigan has 4,162 approved maternity beds in 238 hospitals, the Michigan Department of Health reported. The number of beds has increased by 214 since 1951, the year the state health department was made responsible for licensing hospitals offering maternity service. The health department's minimum rules and standards for maternity hospitals now list 180 regulations, including 122 requiring immediate compliance for a full license. Early compliance will be required on the other regulations, most of which demand capital outlays or long-range planning. Dr. Albert E. Heustis, Lansing, is state health commissioner.

Symposium on Anti-Bacterial Therapy.—The Michigan and Wayne County Academies of General Practice, will present a Symposium on Anti-Bac-

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terial Therapy at the Sheraton–Cadillac Hotel, Detroit, Sept. 12. Two panel discussions are planned, the second of which will conclude the program. Speaker at the luncheon will be Dr. Carroll L. Whitten, Louisville, Ky., vice-speaker, congress of delegates, American Academy of General Practice, presenting, "Freedom of Choice." The program includes the following papers and speakers:

The Management of Hospital Infections, Dr. Wayne W. Glas, Eloise, Mich.
Selection of Antibacterial Agents, Dr. Bert H. Leming, Jr., Memphis, Tenn.
Antibacterial Therapy in the Allergic Patient, Dr. Meryl M. Fenton, Detroit.
The Use of Antibacterial Agents in Obstetrics, Dr. Isadore Dyer, New Orleans.
Anti-Bacterial Therapy in Surgery, Dr. Merle M. Musselman, Omaha.
Childhood Bacterial Infections, William R. Cleaver, Oklahoma City.
Anti-Bacterial Therapy in Urinary Tract Infections, Dr. William J. Martin, Rochester, Minn.
Persistent Resistant Infections, Dr. Aaron Prigot, Forest Hills, N. Y.

No fee is required for scientific sessions, and the program is accepted for five hours category I credit. For information write Dr. Francis P. Rhoades, 970 Maccabees Bldg., Detroit 2.

MONTANA

Annual Meeting in Butte.—The 81st annual meeting of the Montana Medical Association will be held Sept. 17-19 at the Finlen Hotel, Butte. Guest speakers are as follows: Dr. David B. Cheek, San Francisco; Dr. John R. Walsh, Omaha; Dr. Charles W. McLaughlin Jr., Omaha; Dr. John R. Connell, Denver; Dr. Clarence V. Hodges, Portland, Ore.; Dr. Frank W. Newel, Chicago; Thomas F. Dougherty, Ph.D., Salt Lake City; and Dr. John H. Moe, Minneapolis. Dr. Roger W. Clapp, Butte, President, Silver Bow County Medical Society, and Dr. Herbert T. Caraway, Billings, President, Montana Medical Association will open the scientific sessions with addresses. Dr. Louis M. Orr, President, American Medical Association, will be the guest speaker at the annual banquet, Sept. 17, presenting, "Sitting on Top of the World." Technical exhibits, a program of ladies' entertainment, and a golf tournament are arranged. For information, write the Montana Medical Association, P. O. Box 1692, Billings, Mont.

NEW YORK

Hospital News.—A new 20-bed pediatric unit at St. Claire's Hospital, Schenectady, opened its doors to patients recently. Located on the fourth floor, north wing, the new unit formerly served as quarters for the Franciscan Sisters of the Poor, who operate the hospital. The pediatric area has been completely redesigned, remodeled, and equipped for the care and treatment of children. Small infants will have their own nursery of four bassinets with adjacent examination and work rooms. A second nursery has four cribs, and older children occupy three two-bed rooms and two three-bed rooms.

Outbreak of Rabies.—The Veterinary Services Group of the New York State Department of Health reported that this year, as of July 27, rabies had been reported from 16 counties in New York State. There were 64 cases including 11 dogs, 30 foxes, 8 cows, and 15 animals of miscellaneous species. The incidence of cattle rabies reportedly will climb rapidly through November since these animals are now at pasture. Chenango County, with 16 cases reported, has been most heavily infected followed by Wyoming, Livingston, Cortland, Tompkins, and Madison counties. Through May 30, 47 cases were reported this year as compared with 40 for the comparable period in 1958. The report goes on to state that earlier experience with wildlife rabies in Western New York had been limited to a circumscribed outbreak including 15 foxes and one raccoon in Chautauqua County in 1944, single fox cases in 1952 and 1953 in Livingston County, a single fox in Allegany County in 1956, and a fox and a raccoon in Monroe County in 1952 and 1953.

New York City

Eye-Smarting.—The City of New York Department of Air Pollution Control announced that isolated instances of eye-smarting occurred in sections of Manhattan during the morning hours of July 29. A temperature inversion from ground level to 400 feet, combined with extremely low variable winds, caused the discomfort in four different areas, all of them sections of heavy automotive traffic. Complaints began coming into the department at 9 a. m. and continued sporadically until shortly before noon. Field investigations by department inspectors and laboratory technicians revealed slightly above normal levels of pollutants emitted by automotive vehicles.

NORTH DAKOTA

Regional Meeting of Physicians.—The American College of Physicians will hold a regional meeting for North Dakota, Saturday, Sept. 12, in the auditorium of the Provident Life Insurance Building, Bismarck. The American Society of Internal Medicine for North Dakota, will meet in conjunction with the regional meeting, Sept. 11. Dr. H. Marvin Pollard, of Ann Arbor, Mich., regent of the college, will present, "Steroid Therapy in Various Gastrointestinal Problems," and will be the banquet speaker at 7:30 p. m., presenting, "The Responsibility of the American College of Physicians to Foreign Trainees." The program includes the following papers:

North Dakota Coronary Artery Disease Study, Dr. Robert C. Painter, Grand Forks.
Care of the Psychiatric Patient in the Community, Dr. John G. Freeman, Jamestown.
Primary Rheumatic Fever Study: A Preliminary Report, Dr. Walter F. Pretorius, Bismarck.
The Determination of Genetic Sex by Nuclear Chromatism Patterns in Oral Mucosa Smears, Dr. Edwin G. Olmstead, Grand Forks.
Facts and Fallacies with Respect to Etiologoy and Treatment of Arteriosclerosis, Dr. John H. Peters, New York City.
Pregnancy and Diabetes, Dr. Donald M. Barnard, Fargo.
Gastrointestinal Polyposis with Mucocutaneous Pigmentation (Peutz-Jegher Syndrome), Dr. Olaf V. Lindelow, Bismarck.
Review of 1000 Consecutive Electrocardiograms in Clinically Normal and Asymptomatic Males with an Average Age of 50 Years, Dr. Guenther H. Heidorn, Minot.

Registration fee is $10. Dr. Peter R. Gregware, of Bismarck, is the local general chairman.

OHIO

General Practice Meeting in Columbus.—The Ohio Academy of General Practice will hold its ninth annual scientific assembly Sept. 16-17 at the Veterans Memorial Hospital, Columbus. A panel discussion, "Specific Problems Pertaining to the Practice of Industrial Medicine," moderated by Dr. Joseph A. Solomayer, Cleveland, will open the meeting. Papers to be presented by out-of-state speakers are as follows:

GP's Approach to the Parkinsonian Patient, Dr. Kenneth H. Abbott, Los Angeles.
The Allergic Patient, His Problems, Office Diagnosis and Treatment, Dr. John Burger, Birmingham, Mich.
Common Surgical Emergencies, Dr. A. Lee Lichtman, New York City.
Hematuria in Benign Conditions, Dr. Edwin P. Alyea, Durham, N. C.
Management of Frustration in Everyday Practice, Dr. Victor Szyrynski, Ottawa, Canada.

Question-and-answer periods and exhibits are planned. The program is acceptable for 10 hours category I credit for A. A. G. P. members.

Surgeons Meet in Cleveland.—The Ohio Chapter of the American College of Surgeons will meet Sept. 11-12 in association with the Cleveland Surgical Society at the Statler Hilton Hotel, Cleveland. The scientific program will open with addresses by Dr. William B. Holden, president Cleveland Surgical Society, and by Dr. Byron G. Shaffer, president, Ohio Chapter, American College of Surgeons. Guest speakers are as follows: Dr. C. Gardner Child, III, Ann Arbor, Mich.; Dr. Jack Lapides, Ann Arbor, Mich.; Dr. Angus D. McLachlin, London, Ontario; Dr. Rudolf J. Noer, Louisville, Ky.; and Dr. Thomas B. Quigley, Boston. Four panel discussions are arranged under the following titles and moderators: "The Recognition and Treatment of Common Postoperative Complications," Dr. Noer; "Athletic Injuries," Dr. Quigley; "Management of Gastrointestinal Bleeding," Dr. Child; "Current Trends in Cancer Therapy," Dr. Robert M. Zollinger, Columbus. The fourth annual banquet will be held 7:30 p. m., Sept. 11, with Mr. Paul Brown, of the Cleveland Browns, as guest speaker.

OKLAHOMA

General Hospital Dedicated.—The new Muskogee General Hospital was dedicated April 4 with Senator Robert S. Kerr as the principal guest speaker. Following the dedication ceremonies an open house was held for the general public. The Muskogee General Hospital is a nonprofit charitable organization built and owned by the state. It was financed by federal Hill–Burton funds, Memorial Room Furnishing Funds, municipal bond issues and hospital funds. Service needs such as supplies, laboratory, x-ray, sterilization, medical records, and auxiliary needs are provided by a convenient service nucleus. A feature of the new hospital is a central closed circuit broadcasting system and a nurse-to-patient communications system. The new hospital has a minimum of 110 beds and a maximum of 131 beds. Provisions have been made for an additional 60 beds in a three-story addition. The hospital will have a total of 170 beds, with maximum of 200 beds. Facilities include operating and obstetrics suites, a dietary department, pathology department, pharmacy, sterilizing center, medical supply room, central oxygen and suction system, central dictating system, surgeons' dictating room, training and conference rooms, and staff and visitors' lounges, and a central air-conditioning system.

The new Muskogee General Hospital.

WEST VIRGINIA

Annual Heart Meeting.—The annual meeting and scientific session of the West Virginia Heart Association will be held at the Shenandoah Hotel in Martinsburg Sept. 25. Dr. John H. Peters, New York City, assistant medical director of research for the American Heart Association, will speak before the public education session for lay members. The following program has been arranged for the scientific session, the speakers being instructors in medicine at the Johns Hopkins University School of Medicine, Baltimore:

Laboratory Aids in Diagnosis of Coronary Heart Disease and Surgical Therapy of Coronary Heart Disease, Dr. Frank W. Davis Jr.
Diagnosis of Angina Pectoris by Historical Review and

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Dieto-Therapy in Atherosclerosis, Dr. Martin Singewald.
Treatment of Acute Myocardial Infarction and Dietary Approach to Lipid Abnormalities in Atherosclerosis, Dr. Robert Mason.

A panel discussion, "Coronary Heart Diseases, or Atherosclerosis, Its Complications and Management," will be held by the speakers. On Sept. 24, a luncheon will be held at the Shenandoah for volunteers of the association.

Meeting of Chest Physicians.—The annual meeting of the Potomac Chapter of the American College of Chest Physicians will be held at The Greenbrier, White Sulphur Springs, Oct. 9. Dr. William L. Cooke, of Charleston, president of the chapter, will serve as moderator at the morning session which will begin at 9:30 a. m. The following program will be presented at that time:

Tobacco and Cancer, Robert C. Hockett, Ph.D., New York City.
Air Pollution, Mr. O. C. Thompson, South Carleston.
The Pneumoconioses—Diagnosis and Management, Dr. Frank Princi, Cincinnati.
X-Ray Diagnosis of Diffuse Pulmonary Pathology Proven by Lung Biopsy, Dr. Mark H. Wholey, Charleston.

Five papers will be presented at the afternoon session beginning at 2 p. m., with Dr. Milton B. Kress, of Baltimore, vice-president of the chapter, serving as moderator. The speakers and their subjects are as follows:

Coccidioidomycosis, Dr. James H. Matthews, Oteen, N. C.
Blastomycosis, Dr. Harry E. Walkup, Oteen, N. C.
Histoplasmosis, Dr. Timothy Takaro, Oteen, N. C.
The Present Status of the Drugs Used Less Frequently in Tuberculosis, Dr. James H. Matthews, Oteen, N. C.
Open Heart Surgery, Dr. R. Adams Cowley, Baltimore.

A cordial invitation is extended by the chapter to all physicians interested in diseases of the chest. There will be no registration fee.

WYOMING

Fatal Home Accidents.—Home accidents in Wyoming resulted in 304 deaths for the five years of 1953 through 1957. This is an average yearly death rate of 19.9 per 100,000 population compared with the average yearly death rate from this cause of 17.1 for the United States as computed from the National Safety Council reports. The comparison of Wyoming and United States death rates for the major categories for the years 1953-1957 follows:

Home Accident	*Rates per 100,000 population*	
	Wyo.	*U. S.*
Falls	6.9	8.4
Burns	3.7	3.3
Poisoning, solids and liquids	0.6	0.7
Poisoning, gases and vapors	1.9	0.5
Firearms	1.8	0.7
Other	5.0	3.5
Total	19.9	17.1

GENERAL

Meeting of Anesthesiologists.—The second annual conference of the New England Society of Anesthesiologists will be held Sept. 18-19 at the Equinox House, Manchester-in-the-Mountains, Vermont, under the presidency of Dr. Jacob H. Fine, Beverly, Mass. The theme for the conference will be "Agents and Techniques." Speakers are as follows: Dr. Richard G. B. Gilbert, Montreal, Canada; Dr. Harold R. Griffith, Montreal; Dr. William S. Howland, New York City; Dr. Louis R. Orkin, New York City; and Dr. Merel H. Harmel, Brooklyn. Technical exhibits are planned. A golf tournament will be held the afternoon of Sept. 18, and the banquet the evening of Sept. 19.

Symposium on Controlling Disability.—A national symposium on the problem of controlling disability, especially in the areas of cardiac disease, the degenerative diseases of the aged, and psychological disorders, sponsored by the Liberty Mutual Insurance Company as a public service, will be held in Boston, Oct. 15-16. The symposium will consist of medical panels and a series of prepared addresses by leaders from industry, labor, medicine, government, law, and insurance. A highlight of the symposium will be a session devoted to the implications of the latest molecular research as it relates to the connective tissues and the degenerative diseases of the aging. Dr. Rene J. Dubos, of the Rockefeller Institute, will recapitulate the important insights and findings of the symposium in a closing address.

Papers for Symposium on Antibiotics.—On Nov. 4-6, the seventh annual Symposium on Antibiotics, sponsored by the Journals *Antibiotics & Chemotherapy*, and *Antibiotic Medicine & Clinical Therapy*, will be held at the Mayflower Hotel, Washington, D. C. There will be a registration fee of $1. Three copies of abstracts must be submitted by Sept. 14. The abstract should contain about 200 words, and should incorporate where the work was done, what was done, results obtained, and conclusions. An original manuscript and one copy must be submitted by Oct. 15. The manuscript must be original, previously unpublished material. It must be typewritten, double spaced, on one side of 8½ by 11 paper. No more than six illustrations should accompany a manuscript. Generic names of drugs should be used throughout. Send abstracts and manuscripts to Henry Welch, Ph.D., Director, Division of Antibiotics, Food and Drug Administration, U. S. Department of Health, Education, and Welfare, Washington 25, D. C.

Meeting on Poison Control in Chicago.—The second annual meeting of The American Association of Poison Control Centers will be held Oct. 6, at the Palmer House, Chicago. An all-day meeting is scheduled. The morning session will be devoted to

business activities. During the afternoon, papers on research, clinical, and public health aspects of poisoning will be presented and discussed. The association was organized in October, 1958, to "promote the exchange of information among its members on various aspects of acute accidental poisoning." It also expects (1) to promote and encourage investigation into methods for treating such cases of poisoning and (2) to develop educational programs for their prevention. Its members are, for the most part, connected in some capacity with poison control and information centers in the United States and Canada. The majority of the members are pediatricians, although other fields of medicine are also represented. Others include pharmacologists, toxicologists, chemists, and pharmacists. Information may be obtained from Mr. Arthur S. Blan, Secretary-Treasurer pro tem., Connecticut State Department of Health, Hartford 15, Conn.

Meeting of Obstetricians and Gynecologists.—District V of the American College of Obstetricians and Gynecologists will hold its annual meeting in the Statler Hilton Hotel, Detroit, Nov. 18-21. The district comprises Indiana, Kentucky, Michigan, Ohio, and Ontario. Two days will be devoted to the presentation of a scientific program, it was announced by Dr. Edwin S. Hoffman, Detroit, chairman of the program committee. Qualified nurses will be invited to attend the scientific sessions under the sponsorship of fellows in their respective hospitals. The scientific program on Nov. 19 and 20 will consist of five panels, eight scientific papers, and two prize-award papers by residents in obstetrics and gynecology. The annual dinner dance will be held Friday evening, Nov. 20. Dr. Laman A. Gray, of Louisville, will give a historical sketch of Dr. Ephriam McDowell, Kentucky surgeon who 150 years ago performed the first ovariotomy. For information, write Dr. Arthur G. King, District V Chairman, 199 William Howard Taft Road, Cincinnati 19, or to Mr. Donald F. Richardson, Executive Secretary, American College of Obstetricians and Gynecologists, Box 749, Chicago 90.

Poliomyelitis Inoculations.—Though the Salk vaccine was developed and proved effective four years ago, only 67.9 million Americans of a total of 177.3 million have been fully vaccinated against poliomyelitis, Mr. Basil O'Connor, president of the National Foundation, announced. Estimates for July 1, show that 68% of the highly susceptible group of persons under 20 years of age have completed the Salk inoculations. Within this group is the most susceptible of all are preschool children, of whom only 51% completed the Salk shots. In the 20 to 39 age group only 34% have been fully inoculated. Of those over 40, 91% have not been fully vaccinated. Of people who started the series of Salk inoculations but have not yet completed them, 6 million received one shot and nearly 12 million received two. Among those under 20 years of age, the breakdown is 5% receiving one shot and 11% receiving two. The National Foundation also reports that 7.2 million of the 67.9 million persons fully vaccinated went beyond the basic series of three inoculations to take a fourth shot. This booster shot is now recommended by the U. S. Public Health Service and by The National Foundation for persons who completed the basic series at least one year previously.

Military Surgeons Meeting.—Physicians, dentists, veterinarians, nurses, and medical specialist delegates will begin registering for the 66th annual convention of the Association of Military Surgeons on the afternoon of Nov. 8. The theme of the three-day convention is "Practice of Military Medicine—Broadening Concepts." Major Gen. Harold H. Twitchell, MC, USAF, president of the association, will open the meeting Nov. 9. On that afternoon a lecture will be given by Dr. Austin E. Smith, president, Pharmaceutical Manufacturers Association. On Nov. 10, the program will begin with the Porter Lecture, "Trends in Mental Health," by Dr. Paul H. Hoch, New York City, commissioner, Department of Mental Health for the State of New York. A closed circuit color television program will be shown Nov. 10-11. There will be special section meetings with panel discussions for the dentists, veterinarians, nurses, and medical specialists. Films on medical and scientific subjects will be shown continuously throughout the meeting. About 60 technical exhibits and 12 scientific exhibits are planned. There is no registration fee. For information, write the association headquarters, 1726 Eye St., N. W., Washington 6, D. C.

Population Growth Predictions.—California is expected to add more than 6 million inhabitants by 1970 and with a population exceeding 20 million will be the most populous state, according to statisticians of the Metropolitan Life Insurance Company. Other states for which rapid population gains are predicted are Nevada and Arizona, with increases of about 67%, to lead all the states in rate of population growth; Florida, an increase of 40% to bring its population to almost 6 million; and Maryland, Delaware, and Michigan, with increases of at least 33%. For the nation as a whole, including the new states of Hawaii and Alaska, the total population is expected to be over 208,000,000 by 1970, with the annual increment in the intervening years averaging 1.5%. The Metropolitan statisticians base these predictions in part on estimates by the Bureau of Census. Each of the three broad age components of the population will increase, but not in equal measure. Persons at the principal productive ages—18 to 64—will be the slowest growing group; their number is expected to rise only 20% to about 115 million in 1970. The number of persons under 18

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should increase by nearly 25% to about 74 million. At the same time, the over-65 population is expected to increase by 33% to 19.5 million.

Chemical Society Meeting.—The American Chemical Society's 136th national meeting will be held Sept. 13-20, in Atlantic City, N. J. Among the participants will be scientists from Scotland, England, Sweden, France, Japan, and Israel. The program includes 1,589 papers, sponsored by 21 scientific and technical divisions of the society. The Delaware Section of the American Chemical Society will be host to the visiting scientists. A highlight of the meeting will be a general assembly on Monday evening, Sept. 14, in the Ritz–Carlton Hotel at which winners of 13 $1,000 prizes will be announced. Scientific and technical sessions will open at 9 a. m. Monday and continue through Friday. Prof. Roger J. Williams, past-president of the society and director of the University of Texas Biochemical Institute, and Lewis H. Sarett, Ph.D., director of synthetic organic chemistry at the Merck, Sharpe & Dohme Research Laboratories, Rahway, N. J., will address the ACS Division of Medicinal Chemistry, which is celebrating its 50th anniversary this year. C. Chester Stock, Ph.D., of the Sloan–Kettering Institute for Cancer Research and Max Tishler, Ph.D., president of Merck, Sharpe & Dohme Research Laboratories, also will address the Medicinal Division. A symposium on cancer and reports on potential agents to fight diabetes, hypertension, and ulcers are other features. An exhibit of 1,000 books has been arranged by the Division of Chemical Education. A special program of entertainment for women ACS members and wives of members is planned.

Program for Training in Cerebral Palsy.—The United Cerebral Palsy and Education Foundation announced a research and training program including four areas: (1) research and training grants, to support research to increase knowledge of the brain, its functions, and sequelae of alterations thereto, by award of project and program grants; (2) clinical fellowships, to interest young physicians in their residency years, in the problems of diagnosis, clinical management, and periodic follow-up of patients with neuromuscular disabilities; to improve the quality of clinical training in the appropriate medical specialties involved; (3) postdoctoral fellowships in brain research, to support investigators in training in research in neuromuscular disabilities and to improve the quality of such research; and (4) medical student fellowships in cerebral palsy, to interest medical students in diagnosis, therapy, rehabilitation and follow-up of patients with cerebral palsy or in participating in some phase of basic or applied research relating to the problems of brain damage (two to four months). Deadline for submission of applications for funds to be available for Jan. 1, is Sept. 15, and the deadline for funds to be available July 1, is March 15. For information, write the Director of Research, United Cerebral Palsy, Research and Educational Foundation, 321 W. 44th St., New York 36.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	Aug. 8, 1959 Paralytic Type	Aug. 8, 1959 Total Cases	Aug. 9 1958 Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	1
Massachusetts	1	2	1
Rhode Island	..	..	..
Connecticut	10	14	5
Middle Atlantic States			
New York	7	10	10
New Jersey	4	4	16
Pennsylvania	6	10	1
East North Central States			
Ohio	8	17	14
Indiana	2	7	..
Illinois	5	12	5
Michigan	2	11	39
Wisconsin	3	5	2
West North Central States			
Minnesota	6	9	1
Iowa	10	26	1
Missouri	17	28	5
North Dakota	..	..	..
South Dakota	..	2	..
Nebraska	3	10	..
Kansas	1	11	3
South Atlantic States			
Delaware	..	..	3
Maryland	1	1	..
District of Columbia	..	..	..
Virginia	15	40	7
West Virginia	2	2	3
North Carolina	21	23	8
South Carolina	1	1	..
Georgia	10	13	..
Florida	6	11	9
East South Central States			
Kentucky	5	5	..
Tennessee	9	10	8
Alabama	16	19	3
Mississippi	4	8	12
West South Central States			
Arkansas	12	17	..
Louisiana	4	5	1
Oklahoma	10	19	4
Texas	22	41	17
Mountain States			
Montana	..	..	2
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	..
New Mexico	2	3	2
Arizona	3	4	1
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	6	..
Oregon	3	8	..
California	14	17	4
Alaska	..	1	..
Hawaii	..	..	4
Territories and Possessions			
Puerto Rico	..	..	2
Total	245	432	203

Fellowships for Nuclear Training.—The International Atomic Energy Agency offers the following opportunities for training in the peaceful uses of atomic energy at universities, technological institutes, laboratories and other institutions in various member states:

General Techniques Training: to develop skills in the use of some fundamental techniques in the field of nuclear energy.

Specialist Training: to prepare specialists in the theoretical and experimental aspects of the science and technology of nuclear energy.

Research Training: to provide advanced training, including active participation in research work for persons potentially qualified to develop and carry out research programs in the basic sciences and engineering.

Subjects included are: nuclear physics, production, handling, and application of isotopes, research and power reactors, nuclear chemistry, reactor materials, and health physics and protection. Types of fellowships available include (1) Short-term Special Training: for graduates from a university or a technical school of university or equivalent level; (2) Advanced and Research Training: for graduates from a university or a technical school or university or equivalent level (in some cases previous experience in the field of nuclear science and technology will be required); and (3) Long-term complete University Training: for undergraduates possessing a secondary school certificate, to receive general and specialized training in the peaceful applications of atomic energy. All applications must be submitted to the International Atomic Energy Agency through governmental channels exclusively, and candidates must be approved and nominated by their governments. Detailed information is contained in the brochure, "Nuclear Science Fellowships," IAEA Vienna, December 1958, available at the appropriate ministry or government department in each member state.

LATIN AMERICA

El Salvador Medical School.—The University of El Salvador, San Salvador, is developing those departments of its School of Medicine which give training in the basic sciences. The Rockefeller Foundation gave $171,000 for the use of these departments in 1957 and is supplementing this amount in 1959. With the appointment of additional faculty members in the past few years, active programs of research and teaching have been developed in biochemistry, pathology, microbiology, and pharmacology. A department of preventive medicine has been established and will be expanded in the coming years, as will a new teaching health center and outpatient facility adjoining the medical school.

Ophthalmologists Meet in Venezuela.—The sixth Pan American Congress of Ophthalmology will be held in Caracas, Venezuela, Jan. 31-Feb. 6, 1960, according to Dr. Brittain F. Payne, New York, president, Pan American Association of Ophthalmology. The Caracas committee for the congress has sent the following information for those who are making plans to attend: Caracas is situated at an altitude of 2,000 feet, with an average temperature in January and February of 68 F. There is no duty on personal possessions such as clothing, cameras, and projectors. Documents necessary for entrance into the country are: passport, visa, and certificate of vaccination against smallpox. Hotel and travel reservations should be channeled through Dr. William L. Benedict, 15 Second St., S. W., Rochester, Minn., chairman, Committee on Transportation. The scientific meetings of the congress are to be held in "University City," in which there is a large auditorium equipped for simultaneous translation of papers. The program, arranged by Dr. James H. Allen, New Orleans, will be made up of symposiums, round-table discussions, free papers, and motion pictures. The Caracas committee has planned a social program, which will include a dinner at the top of Mount Avila.

FOREIGN

British Library Available to Foreign Doctors.—The Council of the British Medical Association announced that the library facilities of the British Medical Association are available to members of associations that hold membership in the World Medical Association. Foreign doctors resident in Great Britain for a period of not more than six months are invited to use the library facilities. They will be afforded all privileges of these facilities with the exception of borrowing the books. This is an additional project in the program of the British Medical Association in fulfilling the objective of the World Medical Association in promoting contacts between the medical profession in different countries.

Swedish Committee on Health Museums.—Dr. Bruno Gebhard, director, Cleveland Health Museum, recently met with several members of the Swedish National Committee on Health Museums, of which Mrs. Nancy Erikson, member of the Swedish Parliament, is chairman. Other members are Dr. Malcolm P. V. Tottie, from the Swedish National Medical Board; Dr. Lars Anders W. Kock, medical director of the Scandinavian Phillips Organization. The first health museum in Sweden might be located in Stockholm or in Gothenberg, where a new medical school has just been established. Main promoter of a health museum is Dr. Johan Wintzel. Financial support has been promised by one of the Swedish life insurance companies, the Foersakring Folksam.

Civil Defense Conference in Paris.—The Fourth International Civil Defense Conference will be held in the Palais d'Orsay, Paris, France, Sept. 28-Oct. 3. The conference will present a selection of technical equipment from various countries which will include demonstrations. The program includes four topics: atomic hazards; practical civil defense training of the population; juridical status of civil defense personnel and distinctive emblem; and present position of the protection of cultural property. Working parties corresponding to the items on the agenda will be held simultaneously. Film showings are planned and a program of tours

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is arranged. A special program will be scheduled to be held during the conference for persons accompanying delegates. Working languages are English, French, and German with simultaneous translation. For information, write The Secretariat of the Conference, at the Secretariat General of the I. C. D. O., 7 Bd. Jaques-Dalcroze, Geneva, Switzerland.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Various Centers: Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing applications was June 22. Succeeding examinations—March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 21-23, 1960. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

ALASKA:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

ARIZONA:* *Examination.* Phoenix, Oct. 14-16. *Reciprocity.* Phoenix, Oct. 17. Ex. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

ARKANSAS:* *Examination and Reciprocity.* Little Rock, Nov. 5-6. Sec., Dr. Joe Verser, Harrisburg.

CALIFORNIA: *Written.* Sacramento, October 19-22. *Oral.* San Francisco, November 14. *Oral and Clinical.* San Francisco, Nov. 15. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

DISTRICT OF COLUMBIA:* *Examination.* Washington, Dec. 14-15. *Reciprocity.* Washington, Sept. 14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

FLORIDA:* *Examination.* Miami Beach, Nov. 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

GEORGIA: *Examination and Reciprocity.* Atlanta, Oct. 13. Sec., Mr. Cecil L. Clifton, 224 State Capitol, Atlanta 3.

GUAM: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

INDIANA: *Examination.* Indianapolis, June 1960. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

KANSAS:* *Examination and Reciprocity.* Kansas City, January 1960. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

LOUISIANA: *Examination and Reciprocity.* New Orleans, Dec. 3-5. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

MARYLAND: *Examination.* Baltimore, Dec. 8-11, Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

MICHIGAN:* *Examination.* Lansing, Oct. 26-27. Ex. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., Lansing.

MINNESOTA:* *Examination,* Jackson, June 1960. *Reciprocity.* Jackson, Dec. 7. Sec., Dr. A. L. Gray, old Capitol, Jackson.

MINNESOTA:* *Examination and Reciprocity.* St. Paul, Oct. 20-22. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: *Examination and Reciprocity.* Helena, Oct. 6. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

NEW JERSEY: *Examination.* Trenton, Oct. 20-23, *Reciprocity.* Monthly, Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton.

NEW MEXICO:* *Examination and Reciprocity.* Santa Fe, Nov. 16-17. Sec., Dr. C. Derbyshire, 227 East Palace Ave., Santa Fe.

NEW YORK: *Examination.* Albany, Buffalo, New York and Syracuse, Dec. 8-11. Sec., Dr. Stiles D. Ezell, 23 South Pearl St., Albany.

OHIO: *Examination.* Columbus, Dec. 15-17. *Endorsement.* Columbus, Oct. 5. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OREGON:* *Examination.* Portland, Oct. 22-24. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

TENNESSEE:* *Examination.* Memphis, Sept. 23-24. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

TEXAS:* *Examination.* Fort Worth, Dec. 3-5. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

VIRGINIA: *Examination and Reciprocity.* Richmond, Dec. 2-4. Address: Board of Medical Examiners, 631 First St. S. W., Roanoke.

VIRGIN ISLANDS: *Examination.* Charlotte Amalie, Nov. 12-13. Sec., Dr. Benjamin Nath, Charlotte Amalie, St. Thomas.

WYOMING: *Examination and Reciprocity.* Cheyenne, Oct. 5. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination and Reciprocity.* Juneau, November. Sec., Dr. R. Harrison Leer, Alaska Office Bldg., Juneau.

ARIZONA: *Examination.* Tucson, Sept. 15. Sec., Mr. Herman E. Bateman, University of Arizona, Tucson.

CONNECTICUT: *Examination.* New Haven, Oct. 10. Exec. Asst., Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* Washington, Nov. 23-24. *Reciprocity.* Washington, Sept. 14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

KANSAS: *Examination.* Pittsburg, Nov. 6-7. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburg.

MICHIGAN: *Examination.* Ann Arbor and Detroit, Oct. 9-10. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

MINNESOTA: *Examination.* Minneapolis, Oct. 6-7. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEW MEXICO: *Examination.* Santa Fe, Oct. 18. *Reciprocity.* Santa Fe, Oct. 7. Sec., Mrs. M. Cantrell, P. O. Box 1522, Santa Fe.

OKLAHOMA: *Examination.* Oklahoma City, Sept. 25-26. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, Sept. 12. Sec., Mr. Earl M. Pallett, Eugene.

SOUTH DAKOTA: *Examination.* Vermillion, Dec. 4-5. Dr. Gregg M. Evans, 310 East 15th St., Yankton.

TEXAS: *Examination.* Austin, Oct. 12-13. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: *Examination.* Madison, Sept. 11 and Milwaukee, Dec. 5, Sec., Mr. Wm. H. Barber, 621 Ranson St., Milwaukee.

*Basic Science Certificate required.

DEATHS

Abercrombie, Thomas Franklin Ⓜ Decatur, Ga.; born in Douglasville, June 5, 1879; Atlanta College of Physicians and Surgeons, 1903; director of public health, state department of public health for many years; past-president of the Conference of State and Provincial Health Authorities of North America; won the L. G. Hardman Cup, presented by the Medical Association of Georgia for "distinguished service to public health"; member of the Rockefeller Sanitation Commission from 1911 to 1913 and commissioner of health of Brunswick and Glynn County from 1914 to 1917; in 1937 received the honorary degree of doctor of science from Emory University; in 1924 was appointed by the Surgeon General, U. S. Public Health Service, to represent the United States at the International Congress on Public Health and Preventive Medicine held at The Hague; died June 14, aged 80.

Angell, Frank Cassell Ⓜ Randolph, Vt.; Baltimore Medical College, 1894; past-president of the Vermont State Medical Society; veteran of World War I; served as president of the staff of the Gifford Memorial Hospital, where he died June 9, aged 88.

Bantleon, Verne Henry, Topeka, Kan.; University of Kansas School of Medicine, Kansas City, 1906; veteran of World War I; a police surgeon in Kansas City from 1906 to 1909; died in the Veterans Administration Hospital June 18, aged 76.

Bernstein, James, Brooklyn; Long Island College Hospital, Brooklyn, 1911; Eclectic Medical College of the City of New York, 1898; served in France during World War I; a founder of Maimonides Hospital; director of the United Hias Service; died June 28, aged 84.

Bradshaw, Raymond Watson, Massillon, Ohio; Harvard Medical School, Boston, 1923; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; veteran of World War I; served as president of the American Student Health Association; for many years physician to Oberlin College, Oberlin, Ohio; a resident physician at the Massillon State Hospital; served on the staff of the Abilene (Texas) State Hospital; died in the Massillon City Hospital June 10, aged 66.

Card, Horatio Smith, Goffstown, N. H.; Medical School of Maine, Portland, 1899; died June 22, aged 92.

Ⓜ Indicates Member of the American Medical Association.

Chapman, Warren Browning, Joplin, Mo.; Washington University School of Medicine, St. Louis, 1919; veteran of World War I; died June 10, aged 69.

Compton, Arthur George Ⓜ Colonel, U. S. Army, retired, Washington, D. C.; George Washington University School of Medicine, Washington, D. C., 1907; entered the regular Army as a major on Oct. 12, 1920, and retired Nov. 30, 1945; veteran of World Wars I and II; at one time associated with the Wisconsin State Tuberculosis Sanatorium in Wales; died in the Walter Reed Army Hospital June 19, aged 77.

Cullom, Marvin McTyeire Ⓜ Nashville, Tenn.; born in Woodford, Tenn., Nov. 9, 1868; Vanderbilt University School of Medicine, Nashville, 1896; professor emeritus of clinical otolaryngology at his alma mater, where he was a life trustee; trustee at the Webb School, Joint University libraries, Peabody College and Scarritt College; member of the medical advisory board during World War I; specialist certified by the American Board of Opthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society, American Geriatric Society, Pan-American Association of Ophthalmology, Delta Kappa Epsilon, Alpha Kappa Kappa, and Alpha Omega Alpha; fellow of the American College of Surgeons; member of the House of Delegates of the American Medical Association in 1923, 1925, 1928, and 1929; past-president of the Nashville Academy of Medicine, Davidson County Medical Society, Nashville Academy of Ophthalmology and Otolaryngology, and the American Medical Golfing Association; a colonel in the Tennessee National Guard on the staff of former Governor Prentice Cooper, and was commissioner of the state of Tennessee to the New York World's Fair; consulting oculist, Louisville and Nashville Railroad; associated with Nashville General Hospital and St. Thomas Hospital, where he died June 29, aged 90.

Daigle, L. Stanley, Kansas City, Mo.; Meharry Medical College, Nashville, Tenn., 1931; associated with the Queen of the World Hospital, Kansas City General Hospital number 2, and Wheatley–Provident Hospital; died June 5, aged 56.

Erickson, Reuben Johan, Santa Fe, N. M.; born in Galesburg, Ill., Dec. 31, 1888; Johns Hopkins University School of Medicine, Baltimore, 1916; member of the American College of Chest Physicians, American Trudeau Society, and the American

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Clinical and Climatological Association; treasurer, New Mexico Tuberculosis Association; served as associate professor of medicine at the University of Cincinnati College of Medicine and at the Albany (N. Y.) Medical College; at one time director of the Albany County (N. Y.) Tuberculosis Association; veteran of World War I; formerly on the staffs of the Cincinnati Tuberculosis Sanatorium and the Metropolitan Life Insurance Company Sanatorium in Mount McGregor, N. Y.; for many years associated with the Albany (N. Y.) Hospital; died June 5, aged 70.

Fowble, Cyril Elmo, Upperco, Md.; University of Maryland School of Medicine, Baltimore, 1910; died June 11, aged 84.

Fraley, Frederick, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1899; veteran of World War I; associated with the Children's and Pennsylvania hospitals; died June 25, aged 83.

Gray, Thomas W., Nevada, Mo.; St. Louis College of Physicians and Surgeons, 1895; also a pharmacist; died in the City Hospital May 27, aged 92.

Hargreaves, John Morris, Major General, U. S. A. F., Medical Service, retired, Portland, Ore.; born in La Moille, Ill., Feb. 26, 1901; University of Minnesota Medical School, Minneapolis, 1925; commissioned in the U. S. Army in 1925; transferred to the U. S. Air Force on Oct. 11, 1949; retired Nov. 30, 1954; served as command surgeon of the Far East Air Forces in Japan, first deputy surgeon general of the U. S. Air Force, and during World War II was surgeon of the Air Materiel Command; formerly head of the department of ophthalmology and otolaryngology at the Air Force School of Aviation Medicine; during his career held other command surgeon assignments in the United States and abroad; decorations included the Legion of Merit, Bronze Star, Commendation Medal, and numerous campaign and occupation ribbons; appointed medical representative of the civil defense medical department; specialist certified by the American Board of Preventive Medicine; member of the Aero Medical Association, of which he was formerly a member of the executive council; member of the Association of Military Surgeons of the United States; fellow of the American College of Surgeons; died June 2, aged 58.

Heiss, Harry Ⓜ Chicago; Chicago Medical School, 1920; member of the American Academy of General Practice and the Association of Military Surgeons of the United States; veteran of World War I; member of the staff of the Edgewater Hospital, where he died June 27, aged 66.

Helwig, George Freeman Ⓜ Santa Ana, Calif.; University of Kansas School of Medicine, Kansas City, Kan., 1932; veteran of World War II; formerly practiced in Topeka, Kan., where he was for some time president of the staff of St. Francis Hospital; died June 17, aged 52.

Hummel, Walter Leslie, Chicago; Northwestern University Medical School, Chicago, 1953; certified by the National Board of Medical Examiners; interned at the Wesley Memorial Hospital, where he served a residency and where he died June 29, aged 31.

Jones, John Peachey Ⓜ Los Angeles; University of Virginia Department of Medicine, Charlottesville, 1908; veteran of World War I; died May 15, aged 74.

Kennedy, Francis Lawrence Ⓜ St. Louis; St. Louis University School of Medicine, 1930; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; senior instructor in otolaryngology at his alma mater; associated with Firmin Desloge, St. John's, and St. Mary's hospitals; died in St. John's Hospital June 13, aged 55.

Klein, Albert Daniel Jr., Chisholm, Minn.; University of Minnesota Medical School, Minneapolis, 1930; member of the school board; veteran of World War I; associated with Hibbing General Hospital and the Chisholm Memorial Hospital, where he died June 16, aged 61.

Lamb, Ellis Ⓜ Clinton, Okla.; Memphis (Tenn.) Hospital Medical College, 1905; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the consulting staff, Western Oklahoma State Hospital; died in Oklahoma City June 14, aged 81.

Lawlor, William Henry Ⓜ Mahanoy City, Pa.; Temple University School of Medicine, Philadelphia, 1924; president of the city board of education; staff member of the Locust Mountain Hospital in Shenandoah; died June 14, aged 60.

McCaffrey, Lawrence Edward, Manset, Maine; McGill University Faculty of Medicine, Montreal, Que., Canada, 1921; veteran of World War II; died in Bar Harbor June 18, aged 62.

Mastrobuono, Vincenzo di Guiseppe, Hackensack, N. J.; Regia Università degli Studi di Catania. Facoltà di Medicina e Chirurgia, Italy, 1899; died while vacationing in Italy May 9, aged 85.

Maxwell, Charles Wendell, Philadelphia; Howard University College of Medicine, Washington, D. C., 1904; died June 28, aged 80.

Meadors, Hudson L., Nashville, Tenn.; Meharry Medical College, Nashville, Tenn., 1917; served on the faculty of his alma mater; past-president of the alumni association of his alma mater; school phy-

sician for the Tennessee Vocational School for Girls and the National School of Business; died in the Hubbard Hospital June 20, aged 68.

Meirowitz, Philip, North Tarrytown, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1890; formerly a member of the board of education in New York City; died in the United Hospital in Port Chester June 20, aged 90.

Merrill, Leslie Shepard, Ogden, Utah; Western Reserve University School of Medicine, Cleveland, 1917; fellow of the American College of Surgeons; veteran of World War I; on the staff of the Dee Memorial Hospital; died in St. Benedict Hospital June 17, aged 67.

Mitchell, Oliver T. Ⓜ Plano, Texas; American Medical College, St. Louis, 1905; died in St. Paul Hospital, Dallas, June 8, aged 78.

Monroe, Matthew William Ⓜ Milwaukee; Marquette University School of Medicine, Milwaukee, 1944; specialist certified by the American Board of Internal Medicine; clinical instructor in medicine at his alma mater; veteran of World War II; associated with St. Michael's and St. Mary's hospitals; died June 14, aged 40.

Moore, Donald Edmund Ⓜ Eugene, Ore.; University of Oregon Medical School, Portland, 1936; interned at the University of Oregon Medical School Hospitals in Portland; served a residency at the Children's Orthopedic Hospital in Seattle and the Milwaukee County Hospital in Wauwatosa, Wis.; specialist certified by the American Board of Orthopaedic Surgery; member of the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; veteran of World War II, and awarded the Bronze Star; member of the staff of the Sacred Heart General Hospital; died in Nelscot June 14, aged 45.

Morrow, James Joseph Ⓜ North Hollywood, Calif.; University of Minnesota Medical School, Minneapolis, 1924; veteran of World Wars I and II; past-president of the Hollywood Academy of Medicine and the San Fernando Branch of the Los Angeles County Medical Association; at one time practiced in Austin, Minn., and served as health officer of Mower County; member of the American Academy of General Practice; on the staffs of St. Joseph's Hospital in Burbank and the Presbyterian Hospital–Olmsted Memorial in Los Angeles; died June 11, aged 60.

Movitt, Solomon I. Ⓜ Los Angeles; University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1900; associated with the Cedars of Lebanon Hospital, where he died May 3, aged 82.

Noss, John Cyrus Ⓜ Altoona, Pa.; Jefferson Medical College of Philadelphia, 1920; member of the American Proctologic Society and the American Trudeau Society; fellow of the International College of Surgeons and the American College of Surgeons; veteran of World War I; on the emeritus staff at Altoona Hospital, where he died June 21, aged 66.

Osborne, William Dewey, Bypro, Ky.; University of Louisville School of Medicine, 1924; for many years served on the board of education of Floyd County; died in St. Joseph's Infirmary, Louisville, June 22, aged 61.

Osgood, Alfred Townsend Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1899; specialist certified by the American Board of Urology; member of the American Association of Genito-Urinary Surgeons and the American Urological Association; fellow of the American College of Surgeons; professor emeritus of urology at the New York University College of Medicine; served on the staffs of the French and Bellevue hospitals; died June 20, aged 86.

Ott, Henry Alexander, Detroit; Detroit College of Medicine, 1906; died June 19, aged 91.

Peart, William Arthur Ⓜ Sanborn, N. Y.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1905; health officer for the towns of Niagara and Wheatfield; associated with the Niagara Falls Memorial Hospital, where he served as staff president for a period, and Mount St. Mary's Hospital in Niagara Falls; died June 9, aged 87.

Pike, Elmer Waters, Burlington, Vt.; University of Vermont College of Medicine, Burlington, 1919; veteran of World War I; formerly on the faculty of his alma mater; associated with Fanny Allen Hospital in Winooski, Bishop De Goesbriand Hospital, and the Mary Fletcher Hospital; died June 16, aged 69.

Redmond, Thomas Michael Ⓜ Monticello, Iowa; Northwestern University Medical School, Chicago, 1904; served on the board of education and as city health officer; associated with the John McDonald Hospital, where he was a member of the board of directors; member of the board of directors of the Monticello State Bank; a charter member of the Monticello Rotary Club; died June 13, aged 80.

Rhoads, Cornelius Packard Ⓜ New York, director of the Sloan–Kettering Institute for Cancer Research since its founding in 1945, died suddenly at his home in Stonington, Conn., Aug. 13, aged 61. Dr. Rhoads was born in Springfield, Mass., June 20, 1898. He received a bachelor of arts degree from Bowdoin College in Brunswick, Maine, and was graduated cum laude with a medical degree from the Harvard Medical School, Boston, in 1924. After serving an internship at the Peter Bent Brigham Hospital in Boston, he was appointed a fellow at Trudeau Sanatorium in Saranac Lake, N. Y. He was an instructor in pathology at Harvard Medical

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School from 1926 to 1928 and an assistant pathologist at Boston City Hospital during the same period. In 1928 he joined the staff of the Rockefeller Institute for Medical Research in New York City, where he served as an associate pathologist and associate member in charge of the study of hematologic disorders. In 1940 he was named professor of pathology at the Cornell University Medical College, New York City, and held that post until 1952, when the Sloan-Kettering Division of Cornell University Medical College was created. At that time Dr. Rhoads became professor of pathology in the division's department of biology and growth, a post he held at the time of his death. Dr. Rhoads served since 1953 as scientific director and from 1940 to 1950 as director of the Memorial Center for Cancer and Allied Diseases, of which the Sloan-Kettering Institute is the research affiliate. He was a fellow of the New York Academy of Medicine and served on its committee on public health relations. He was a vice-president of the academy from 1943 to 1945 and was appointed in 1952 to its committee on honorary fellowships. He was a fellow of the American College of Physicians and the American Association for the Advancement of Science, of which he was vice-president and chairman of the section on medical sciences in 1953. He was director from 1941 to 1946 and a member of the executive committee 1944-1946 of the American Cancer Society. Dr. Rhoads held memberships in the American Association for Cancer Research, American Association of Pathologists and Bacteriologists, American Geriatrics Society, American Industrial Hygiene Association, American Public Health Association, American Radium Society, American Society for Clinical Investigation, American Society for the Prevention of Cruelty to Animals, American Society for Experimental Pathology, American Society of Tropical Medicine, Association of American Physicians, Halsted Club, Harvey Society, Inter-Society Cytology Council (founder membership), Interurban Clinical Club, James Ewing Society, New York State Society for Medical Research, Peripatetic Club, Society for Experimental Biology and Medicine, Society of Medical Jurisprudence, Tissue Culture Association, Army and Navy Club, Century Association, Harvard Club of Boston, Society of Sigma Xi (Cornell Chapter), and the University Club in New York. He was the recipient of the Caldwell Medal of the American Roentgen Ray Society in 1942, Clement Cleveland Medal Award by the New York City Cancer Committee in 1948, the American Cancer Society Award in 1955, and the Walker Award of the Royal College of Surgeons the following year. From 1955 to 1957 Dr. Rhoads was a councilor of the New York Academy of Sciences and in 1956 served as chairman of the nominating committee. He was a member of the special committee on cancer control and its special committee on illegal practice of medicine, Medical Society of the County of New York. In 1953 he became a member of the Cancer Chemotherapy Committee and in 1951 was elected a trustee of the Charles F. Kettering Foundation. During World War II he served as a colonel in the Army Medical Corps and chief of the medical division of the Army's Chemical Warfare Service for which he received the Legion of Merit. He was a member of the National Research Council and, during World War II, served as a member of its subcommittee on blood substitutes and as a member of its committee on war gas casualties and as chairman of its blood procurement service. After the war he served as a member of its committee on veterans medical problems, a member of its committee on atomic casualties, and as chairman of its committee on growth. Later in the 1940's he became a member of the council's advisory committee on Chemical-Biological Coordination Center and a member at large of its division of medical sciences. In 1954 he was made an honorary police surgeon by the New York City Police Department and was appointed a consultant in the surgical staff of the Westerly (R. I.) Hospital. He received an honorary doctor of science degree from Bowdoin College in 1944, an honorary doctor of science degree from Williams College in 1952 and an honorary doctor of laws degree from the University of Saskatchewan in 1958. As a result of his experience in the chemical war service during World War II, he became a leader in the development of chemical agents for the selective treatment of cancer. He was known for his work in developing the nitrogen mustard used in the Chemical War Service into a chemotherapeutic agent.

Thompson, John Lee, Wilmot, Ark. (licensed in Arkansas in 1908); died June 4, aged 81.

Wadley, Benjamin Lee, Jackson, Tenn.; College of Physicians and Surgeons, Little Rock, 1909; died June 8, aged 76.

Wiley, Norman Hyde Ⓜ Colonel, U. S. Army, retired, South Mountain, Pa.; born in Hollisterville, Pa., March 24, 1901; Jefferson Medical College of Philadelphia, 1928; commissioned in the medical corps of the U. S. Army in 1929; veteran of World War II; served as post surgeon and hospital commander at Fort Riley, Kan., commander of the U. S. Army Hospital at Fort Benning, Ga., and supervisor of the Gorgas Hospital at Ancon, Canal Zone; formerly commander of Percy Jones Army Hospital at Battle Creek, Mich.; decorations included the Legion of Merit and French Legion of Honor; retired June, 1958, after 30 years service in the Army; member of the board of Franklin County Tuberculosis and Health Society; fellow of the American College of Surgeons; medical director of the Samuel G. Dixon State Hospital, where he died June 10, aged 58.

FOREIGN LETTERS

AUSTRIA

Thyroid Symposium.—H. Egert stated that the thyroid inhibition test is based on the fact that the exogenous supply of thyroxin causes inhibition of the spontaneous activity of the thyroid in healthy persons, while this is not the case in patients with hyperthyroidism. By comparing the storage of radioactive iodine (I^{131}) in the thyroid before and after the supply of hormone, valuable indications for the functional condition of the thyroid may be obtained. A reduction of the 24-hour storage to less than 65% of the initial value is considered normal. For routine diagnosis the more suitable plasma I^{131} test is recommended. In patients in whom, because of a "thyroidectomy effect," a definite result cannot be obtained, diagnostic clarification is usually possible with the aid of the inhibition test.

H. Spitzy said that, based on microanalytic and radioanalytic studies, a simple method of determining the iodine content in only 0.5 cc. of serum had been developed, which could be used for routine tests. With use of this method 10 mg. of sodium iodide, given by mouth, greatly reduced the protein-bound iodine (PBI) level within eight hours. If the inorganic serum iodine level dropped below about 12 mcg. per 100 cc., the PBI value went back again, in a pendulum-like movement.

H. Frischauf reported that in euthyroid persons the determination of PBI in the plasma and the I^{131} test have about the same accuracy, which is relatively high, while the basal metabolism frequently shows an increase due to diseases not depending on hyperthyroidism. For patients who had undergone thyroidectomy the plasma PBI level, if the reduced normal range is taken into account, is the most reliable laboratory method for the evaluation of the thyroid condition; since the I^{131} test, particularly in borderline cases, is not adequate, and for the basal metabolism the previously mentioned limitations must be recognized. In patients with hyperthyroidism the I^{131} test proved to be more accurate. In patients with hypothyroidism both methods showed equally good results. To establish the diagnosis of a functional disturbance of the thyroid it was recommended that the plasma PBI level be determined. If the obtained value lies in the median normal range, a functional disturbance of the thyroid can almost certainly be excluded, in persons who have not yet received treatment. If this value lies on the borderline, then an I^{131} test is required to confirm the clinical diagnosis. For the exclusion of extrathyroid factors the basal metabolism is of supporting significance in making the diagnosis.

K. Fellinger stated that the main difficulties in treating thyroid conditions consist of the differentiation of borderline cases of hyperthyroidism and of establishing indications for various therapeutic measures. Although the I^{131} test provides the most reliable information, one should not overlook the fact that it is concerned with determinations of the iodine metabolism and that errors of interpretation are possible when the results, which are precise concerning the iodine metabolism, are applied to the thyroid function. The purely quantitative concept (hyperfunction or hypofunction) can no longer be maintained, since a large series of indications for possible qualitative changes may result from the formation of the thyroid hormone, its reduction, and its use at the periphery.

At the surgical department of the Empress Elizabeth Hospital 130 patients with goiter, or about 33% of all new patients with goiter, were subjected between Dec. 1, 1957, and Dec. 31, 1958, to roentgenographic examination of the thyroid at the isotope laboratory. Among them were 68 with "cold" adenomas and 14 with "hot" adenomas. Of the latter 10 could be subjected to a conservative operation, i. e., enucleation of the hyperactive adenoma without impairment of the rest of the organ. A complete clinical success was obtained. Of 26 with solitary cold adenomas, which on operation were confirmed as isolated, 8 showed beginning malignant degeneration and an additional 10 showed unequivocal malignant degeneration in the absence of clinical indications of blastoma. Of 14 with recurrent goiters 8 showed such small remainders of thyroid tissue on examination that the associated stenosis of the trachea was considered to have originated from cicatrization. In these patients repeated thyroidectomy would have been a failure.

BRAZIL

Feminizing Ovarian Tumors.—Prof. C. Mignoni and co-workers of the University of São Paulo (*An. Clin. ginec. Fac. med. Univ. São Paulo*) studied a series of nine patients with tumors of the ovary. All the patients had predominant thecal tissue over the membrana granulosa. The microscopic study showed different findings, according to the degree of maturation of the thecoma. In five patients most

The items in these letters are contributed by regular correspondents in the various foreign countries.

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of the tumor consisted of fibrous and hyalinized tissue, indicating advanced differentiation. One of these tumors was associated with peritoneal metastases, in spite of the benign histological picture of primitive ovarian tumor it presented. The functional activity of these tumors was evident in two patients who had cystic glandular hyperplasia. In another the tumor was associated with an endometrial carcinoma, which may depend on the hormonal stimulation of the ovarian tumor, according to some authors.

In the same issue Dr. C. A. Salvatore reported a series of 11 feminizing ovarian tumors (5 membrana granulosa tumors and 6 thecomas). These appeared in patients between 30 and 70 years of age. In two patients whose membrana granulosa tumors developed during the reproductive period there were long periods of amenorrhea (9 and 10 months respectively). Two granulosa cell tumors and two thecomas, in menopausal patients, were characterized by metrorrhagia. One thecoma with clinical signs of malignancy was associated with cystadenocarcinoma of the contralateral ovary. The endometrium was examined in six patients and revealed one membrana granulosa tumor associated with cystic glandular hyperplasia of the endometrium. Of the remaining five (with thecomas) two showed endometrial hyperplasia, one an atrophic endometrium, one an endometrium in the proliferative phase, and one associated with malignant adenoma of the endometrium. The treatment consisted of unilateral adnexectomy in the younger patients and bilateral adnexectomy with total hysterectomy and postoperative x-ray treatment in women over 40 years of age.

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CHILE

Typhoid.—Drs. Orozco and Plaza de los Reyes (*Rev. méd. Chile* **87**:266, 1959) studied a series of 95 patients with typhoid. The principal clinical manifestations were fever in 89, palpable spleen in 80, headache in 75, typical changes in the tongue in 68, absence of eosinophils in 52, diarrhea in 49, leukopenia in 41, normochromic anemia in 24, rose spots in 20, and epistaxis in 12. The serologic test (Widal reaction with agglutinins H and O) was positive in 67 patients in the first week of the disease and in 84 in the second week. Blood cultures gave positive results in the first week in 64 but in only 36 in the second week. Complications were infrequent. Only eight had gastrointestinal hemorrhage, four had hepatitis, two had intestinal perforation, two had nephritis, and one had cholecystitis. Chloramphenicol was given in a total mean dose of 28 Gm. The drug terminated the febrile period in an average of four days. The treatment was continued for an average of 11 days. Relapses were observed in only six, and only two patients died.

The authors compared the symptoms and course of the disease in this antibiotic era with those in the preantibiotic era. In the present series the complications were fewer and less severe. None developed meningitis, thrombophlebitis, periostitis, neuritis, pneumonia, or arthritis. The percentage of relapses was also smaller. Relapses can be prevented by continuing drug administration. If a relapse does occur, it can be controlled by resumption of the therapy. The drug was well tolerated.

Primary Carcinoma of the Liver.—Dooner and Rojas of Santiago (*Rev. méd. Chile* **87**:238, 1959) studied a series of 49 patients with primary carcinoma of the liver. They concluded that the diagnosis of this condition was difficult. The following points should lead the physician to consider it in the differential diagnosis. 1. The patient is 50 or over. 2. He has abdominal pain in the right side, with a rapid accumulation of ascites. 3. He has a stony enlargement of the liver. 4. He has moderate jaundice. 5. He has enlargement of the hepatic shadow on roentgenologic examination. 6. The level of his serum alkaline phosphatase is found to be increasing.

GERMANY

Flatfoot.—R. Penners (*München. med. Wchnschr.* **101**:957, 1959) suggested early performance of the operation devised by Niederecker in children with flatfoot when no relief can be obtained by the application of supports and exercises. The object of this operation is to normalize, as far as possible, the disturbed muscular balance and the alteration of the articular axis by adequate prolongation of the tendons, muscle graft, and osteotomy. After application of a cast, which must remain in position for six weeks, the grafted muscles must be strengthened by exercises. The results of the operation, especially in young persons, are excellent. Of a group of 110 patients so operated on 74 or 67% were able to take up heavy work. Of 76 children who were subjected to this operation 60 were able to do heavy work and 6 light work.

Promazine.—According to G. Janssen and co-workers of Düsseldorf (*Arch. für Kinderh.* **159**:141, 1959) the strong adrenolytic effect of chlorpromazine sometimes causes an orthostatic collapse. Because of the excellent effect of the phenothiazines in soothing the autonomic nerves it proved advantageous to find phenothiazine derivatives with a trivial effect on the circulation. Therefore promazine was chosen from a wide variety of such derivatives. Tests with children whose circulatory system was normal demonstrated that promazine possesses a circulatory tolerance three times greater than that of chlorpromazine. The sedative effect was somewhat less than that of chlorpromazine but the

potentiation of narcotics was equally strong. The sedative effect of oral doses proved nearly as strong as that of intramuscular injections, which means an excellent resorption of the compound. No side-effects are usually seen with doses up to 3 mg. per kilogram of body weight. This dose may be repeated after four hours because of the rapid elimination of the drug.

Psoriasis Vulgaris.—Due to the uniform symptoms of psoriasis vulgaris the nondermatologist is well acquainted with its clinical features. According to T. Grüneberg of Halle (*München. med. Wchnschr.* **101**:1149, 1959) only quantitative and qualitative deviations of these features (psoriasis limited to atypical sites, erythrodermic psoriasis, and exudative or pustular psoriasis) may cause diagnostic difficulties. The liability to psoriatic reactions is irregularly dominant, hereditary, varies widely, and strongly depends on conditional factors, elimination of which is important for therapy. Whether the still unknown underlying cause is in any way connected with the carbohydrate or fat metabolism is not known. A possible causal connection with the function of the adrenal cortex was pointed out by the author for the first time in 1934. In recent years scientific interest has been focused on the processes in the skin. The parakeratotic cornification and the epidermal protein metabolism especially were the centers of investigation. Whereas Paschoud and co-workers noted inhibition of several tripeptidases in the epidermis of psoriatic skin, the activity of another tripeptidase (de-alanylglycylglycin) was significantly increased. The increase of the epidermal dehydrogenase or succinic acid dehydrogenase reaction, which occurs as the first symptom of a mechanically elicited isomorphic irritative effect, seems to suggest the primary commencement of the psoriatic reaction in the epidermis.

Epidermoid (Squamous Cell) Carcinoma of the Cervix Uteri.—The diagnosis of surface carcinoma or "markedly atypical epithelium" was made in 50 patients of the University Women's Clinic, Göttingen, by Kirchhoff and Witt (*Deutsche med. Wchnschr.* **84**:979, 1959). More detailed diagnostic procedures revealed carcinomatous infiltration in 13 of these. It was pointed out that two prognostically different conditions may have a similar histological appearance: (1) the edges of an actively growing infiltrating epidermoid (squamous cell) carcinoma and (2) the surface carcinoma which is capable of regression. If, after amputation of the cervix, a true carcinoma is histologically demonstrated, radical operation or combined radium and x-ray therapy are indicated.

Hormone Treatment for Mammary Carcinoma.—T. Hornykiewytsch of Giessen (*Strahlentherapie*, vol. 109, 1959) reported a series of 260 patients with generalized carcinoma of the breast who had symptomatic treatment (group 1), x-ray castration (group 2), therapy with testosterone (group 3), and therapy with methandriol (group 4). The average survival time of all patients (improved and unimproved) was 5.6 months in group 1 (control group), 7.6 months in group 2, 9.9 months in group 3, and 7.5 months in group 4. Of those in whom objective improvement could be detected the survival time in group 2 was 12.5 months; in group 3, 17.2 months; and in group 4, 12 months. If only symptomatic improvement occurred the survival time in group 2 was 7.2 months; in group 3, 11.8 months; and in group 4, 7.0 months. The prolongation of the average survival time of the differently treated patients was therefore significant. Their survival time was twice or three times longer than that of the untreated patients. The mode of action and the value of x-ray castration, oophorectomy, adrenalectomy, hormone treatment, and hypophysectomy was analyzed. The author concluded that the patient with metastasizing mammary carcinoma should be treated with x-ray castration and administration of hormones. If this is not effective a radiohypophysectomy should be accomplished.

INDIA

Prostatic Malignancy.—Deodhare and Mordecai (*Current Medical Practice*, vol. 3, May, 1959) reported the incidence and various pathological patterns seen in prostates examined during a period of seven years. Of 210 specimens 19 or 9% showed carcinoma, 179 benign hypertrophy, 4 fibrosis, 3 acute prostatitis, 2 leiomyomas, 1 tuberculous prostatitis, 1 prostatic abscess, and 1 myxosarcoma. The presenting symptoms were difficulty in micturition, frequency of micturition, retention of urine, and hematuria. The patient with myxosarcoma had painless hematuria as the only clinical symptom. Those with tuberculous and acute prostatitis were diagnosed clinically as having malignancy of the prostate, the correct diagnoses being made only on histological examination. The maximum incidence of benign hypertrophy was found in the group of those aged 51 to 70 years, the youngest patient being 32 years of age.

The incidence of carcinoma was high in the group aged 51 to 60 years, and the youngest patient in this series with carcinoma was 42 years of age. Myxosarcoma of the prostate occurred in a young man aged 23. Leiomyoma was found in the group of those aged 51 to 60 years. The carcinomas were histologically classed as adenocarcinoma (14), spheroidal cell carcinoma or medullary carcinoma (3), squamous cell carcinoma (1), and giant cell carcinoma (1). Five adenocarcinomas were associated with benign enlargement of the prostate. In

four of them the carcinomatous tissue was distinct from the benign hypertrophy, while in one a transition from carcinomatous cells to those of acini of benign hypertrophy was demonstrated.

Serpina and Hypertension.—Gour and Mital (*Current Medical Practice*, vol. 3, May, 1959) studied three groups of three 8-week-old chicks each for a period of 24 weeks. The chicks were kept on a diet of cereal supplemented with multivitamin drops. One group served as controls and received tap water to drink. In the second group 0.9% saline replaced the tap water, while the third group, in addition to sodium chloride solution, received serpina (a crude preparation of Rauwolfia serpentina) in a dose of 7 mg. per pound of body weight. The general condition of the chicks was noted. The blood pressure was recorded at 6, 12, 18, and 24 weeks. Other investigations repeated every six weeks included total plasma cholesterol (C) and total plasma lipid phosphorus (P) levels and the C:P ratio. Autopsy was performed at the end of the period of observation and the condition of the heart, brachiocephalic trunk, thoracic aorta, and abdominal aorta was studied.

The normal range of blood pressure in the control group varied between 112 and 136 mm. Hg systolic and 92 and 116 mm. Hg diastolic. The total plasma cholesterol level in this group ranged between 102 and 118 mg.% and the plasma lipid phosphorus level between 7.3 and 8.4 mg.%. The C:P ratio was between 13.2 and 14.7. In the second group fed with salt water hypertension was induced, affecting both the systolic and diastolic readings. The maximum level of blood pressure was 168 mm. Hg systolic and 140 mm. Hg diastolic. The rest of the values were unaltered, and no atherosclerotic changes were noticed. In the third group administration of serpina along with salt water prevented the occurrence of hypertension. Other values were also unaffected.

Chronic Duodenal Ulcer.—A. L. Som (*Calcutta Medical Journal*, vol. 56, May, 1959) suggested a Heineke-Mikulicz type of pyloroplasty and vagotomy for early duodenal ulcers situated in the anterior wall. Pyloroplasty is not possible when the ulcer is not exactly in the anterior wall and the pyloroduodenal junction is deformed. In such cases a localized excision of the ulcer, the anterior segment of the pyloric sphincter, and part of the antrum, followed by reconstruction, is recommended. The continuity after such an excision can be maintained by keeping a strip of the posterior wall of the junction, which also prevents leakage. A fairly wide stoma can be made, during reconstruction of the gastroduodenal tract, by a plastic procedure in which a part of the anterior wall of the stomach is swung to the right to fill up the gap. This is further facilitated by incising the anterior wall of the duodenum in a downward and anterior direction.

Ulcers of the posterior wall are usually posterosuperior or posteroinferior and can be treated by a pyloroduodenoplasty. In most patients with pyloric stenosis there is partial stenosis with scarring of part of the circumference when a localized excision and plastic reconstruction are performed. If the stenosis is complete, excision of a dumbbell-shaped segment with reconstruction of the gastroduodenal tract as in the Billroth 1 type of gastrectomy is performed. Vagotomy as a supplementary measure is performed when the free hydrochloric acid level is above 60 degrees. The author reviewed a series of 31 patients with chronic duodenal ulcers on whom the above procedures were performed. There were 13 who had a modified pyloroplasty, combined with vagotomy in 10. Of these three died. Sixteen had a pyloroduodenoplasty, with vagotomy in five. Wedge excision of gastric ulcer with excision of pyloroduodenal stenosis and Billroth 1 reconstruction was performed on one patient, and one had excision of dumbbell-shaped segment with pyloroduodenal stenosis and Billroth 1 reconstruction.

The follow-up study of these patients included clinical examination, radiologic findings, and fractional test meal examinations. One patient complained of occasional acidity and epigastric fulness. One developed a small leakage and three of the earlier cases had some gastric stasis, which improved within six months. The rest of the patients were doing well, had gained weight, and had a good appetite when last seen. A fractional test meal showed diminished acidity. A "barium meal" showed no gastric stasis. Of the three who died, death in one was due to internal hemorrhage from an esophageal varix, in the second to profuse hematemesis on the 11th postoperative day, and in the third to uremia from postoperative electrolytic imbalance. A long-term follow-up study is necessary for correct evaluation of the procedure, but if there is a recurrence gastrectomy is still possible.

Prolonged Use of PAS.—S. Chandra and co-workers (*Journal of the Indian Medical Association*, vol. 32, June, 1959) stated that several reports of the occurrence of jaundice in patient receiving para-aminosalicylic acid (PAS) have appeared. The authors noted marked glycogen infiltration of the liver in albino rats receiving PAS in a previous experimental study. This was followed by a clinicohistological study of the livers of patients who were given PAS alone for prolonged periods; 38 patients were thus studied. Of these 25 suffered from pulmonary tuberculosis and received 12 to 16 Gm. of PAS a day for four to six months and no other drug. The rest suffered from such diseases as anxiety neuroses, paraplegia, and skin disorders. PAS was administered to them in the same dosage for three to four

months. The liver became palpable 1 to 1½ in. below the costal margin in seven patients after four months of PAS administration and in six more after six months of this treatment.

Ten of these were tuberculous and three nontuberculous. The liver was firm, not tender, and had a well-defined margin and smooth surface. The diaphragm was found on fluoroscopy to move normally. Results of the thymol turbidity and cephalin and cholesterol flocculation tests were unaltered in most of the patients. There were no significant changes in the serum bilirubin level, total serum protein contents, or the albumin:globulin ratio. There was slight increase in the total serum cholesterol level, but the change was not marked. Liver biopsy performed on seven tuberculous and three nontuberculous patients showed no change in the lobular pattern. Only two of these patients showed mild glycogen infiltration. Thus administration of PAS in a dosage of 12 to 16 Gm. daily for as long as six months did not significantly affect the liver function or liver morphology.

Demographic Advisory Body.—The ministry of health appointed a demographic advisory committee to advise on research and studies in interrelationships between economic, social, and population changes, the reproductive pattern, and attitudes and motivations affecting the size of the family. The committee will advise on training and research in demography, in order to be of assistance to the government in taking economic and social measures. It will also coordinate demographic research schemes, review the progress made at different centers, and examine and recommend proposals submitted to the ministry of health for financial help for demographic research. Four such centers have been set up in Bombay, Delhi, Calcutta, and Trivandrum respectively.

Tuberculosis.—As a public health problem tuberculosis ranks high in India (*The Pharmaceutist,* vol. 5, May, 1959). Owing to the absence of accurate vital statistics and inefficient registration of births and deaths a precise estimate of the number of deaths resulting from tuberculosis is not possible, but the figures available from year to year show that in spite of the preventive and curative measures used the disease is steadily increasing in incidence. In 1935 the recorded number of deaths per year from pulmonary tuberculosis was at least 500,000, for the whole of India. Tuberculosis affected about twice as many people in 1956-1957 as in 1935-1936. The increase was most marked in centers with the greatest commercial and educational development and in the village districts linked with them by direct communication, but recent surveys indicate that people in rural areas are also becoming victims of the disease. Of the three types of infection only the human type is common in India. In some areas the situation is so serious that unless strict measures are taken the entire population may soon be in the grip of the disease. The rate of infection varies from 21 to 34% in rural areas and 80 to 90% in urban areas.

It is not possible to hospitalize all the patients suffering from tuberculosis, and actually this is not necessary. India has a total of 6,000 beds for tuberculous patients. The minimum requirement would be about 1,500,000. To solve this problem, home treatment has been organized on an extensive basis, thus reducing the need for such colossal expansion of hospital facilities as would be needed. All patients requiring medical care come to clinics once a month and also receive a monthly visit in their homes by a physician from the clinic. Visits are more frequent if conditions warrant. Preventive measures are stressed, and contacts are encouraged to come to the clinic for examination. Many patients have been rendered sputum-negative by this treatment, and it has brought to light the presence of active disease in about 12% of the contacts. The campaign for BCG vaccination was another big step forward in fighting tuberculosis. By 1958 90 million people had been tuberculin-tested and 28 million vaccinated. The results obtained with streptomycin and isoniazid, however, have been disappointing. This treatment has created a false sense of security that may have serious consequences. Owing to the absence of a comprehensive tuberculosis service victims of the disease take a few courses of these drugs and thereafter roam about half-cured and still capable of spreading the infection.

Infantile Cirrhosis of Liver.—Mehta and Verma (*Indian Journal of Child Health,* vol. 8, May, 1959) studied a series of 40 infants with cirrhosis of liver. These children had dyspepsia, anorexia, abdominal distention, hepatosplenomegaly, prominent superficial abdominal veins, ascites, and jaundice; 70% had fever. Such obvious causes of liver enlargement as kwashiorkor, chronic malaria, infectious hepatitis, syphilis, congestive heart failure, and severe anemia were excluded. Liver biopsy was performed on 30, after ascertaining that bleeding and clotting time were normal. No accidents resulted from the liver biopsies. Three of the patients were aged under 1 year, the youngest being 3 months of age. A definite familial history was available in only one child, whose twin brother had died of the same disease. Eleven were used to a mixed diet and the rest were vegetarians. Usually solid food was not started in these children until the 3rd year of life, and in some breast feeding was continued until the 5th year. Visibly distended abdominal veins and ascites were terminal manifestations.

It was difficult to correlate the general condition of the patient with the degree of liver involvement. Plasma protein levels were lowered in 80%, but the

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albumin:globulin ratio was altered in only 57.5%, and most of these had advanced cases. The alkaline phosphatase level was normal in 78.4% but very low levels were found in severe cases. Serum cholesterol levels were normal in only nine. Except for alteration of the albumin:globulin ratio and result of the Van den Bergh test, none of the biochemical tests of liver function helped in assessing the prognosis or the stage of liver involvement. Histologically the liver pattern was distorted in all patients. Periportal inflammation was also evident in all. Generalized cell damage was related to an altered albumin:globulin ratio, thymol flocculation, and thymol turbidity. Eleven patients showed reticuloendothelial hyperplasia, which was probably related to the altered albumin:globulin ratio but not to the level of plasma proteins.

Diarrhea in Children.—P. C. Bopaiah (*Indian Journal of Child Health*, vol. 8, May, 1959) stated that diarrhea still constitutes a major pediatric problem. Most acute diarrheas are due to bacillary infection. The author studied 50 cases of acute diarrhea in children under 2 years of age. Only those with more than six stools a day were included, and those with long-standing diarrhea and malnutrition were excluded; 27 had more or less severe diarrhea with moderate or severe dehydration. The stools showed a heavy exudate of pus cells and streaks of blood. Seven children had such parenteral infections as bronchopneumonia, acute otitis media, or umbilical sepsis, and all of these had a temperature of 100 to 104 F (37.8 to 40 C). Only one child in this group showed severe dehydration.

Stool cultures were made in 19 cases; 13 of these showed a pure growth of Escherichia coli. Other specimens showed Streptococcus faecalis and Staphylococcus aureus, with or without Esch. coli. Only one yielded Shigella flexneri. Treatment consisted of rehydration, feeding, and chemotherapy. Fluids were given by either oral, subcutaneous, or intravenous routes. Saline solution with 5% dextrose was used for infusions. In children with moderate and severe dehydration 2 Gm. of potassium chloride was given orally in two doses, after it was ascertained that the urinary output was adequate. The drugs used were procaine penicillin, streptomycin, sulfaguanidine, and a compound of neomycin and pectin. Sulfaguanidine, which was given to five patients, proved to be unsatisfactory. Streptomycin by mouth was helpful in mild cases. The neomycin-pectin compound gave good results and also helped patients in whom the former two drugs had failed.

Drop Foot.—Transfer of the tendon of the tibialis posterior muscle to correct drop foot has not been popular because of the difficulty of reeducation. Brand and Selvapandian (*Indian Journal of Surgery*, vol. 21, April, 1959) performed this procedure on 108 victims of leprosy, 7 victims of poliomyelitis, and one patient who had had an injury to the lateral popliteal nerve. The authors found that if the postoperative reeducation is carefully carried out, a proper muscle coordination will result after such tendon transfer. The lateral popliteal nerve was involved in all the patients in this series, with loss of function in all the dorsiflexors and peroneal muscles resulting in foot drop, inversion of the foot, and sometimes hammer toes. Ulceration was common under the metatarsal heads in drop foot and on the lateral border of the foot when the foot was inverted. The transfer was done with the use of either the interosseous or circumtibial route, to bring the tendon to the dorsum of the foot. Such forward transfer removes a dynamic deforming factor and helps in active dorsiflexion of the foot. The operation was performed only when there was no open ulcer on the foot and only after a full month had elapsed after healing of the ulcer.

After operation the foot is put in a plaster cast in which a wooden sole-plate and rocker are incorporated. The patient is allowed to walk after four days and the cast removed after six weeks. Weight-bearing exercises are started about 10 days after the foot has come out of the cast. Proper reeducation is essential. Of the patients operated on 39 were followed up for 3 to 27 months. Of the 25 operated on by the interosseous route the results were excellent in 5, good in 12, fair in 7, and poor in 1. The gait was normal in 11, mildly high-stepping in 13, and high-stepping in 1. The circumtibial route was used in 14 patients and the results were excellent in 5, good in 8, and fair in 1; the gait was normal in 11 and mildly high-stepping in 3.

Quality of Human Semen.—S. S. Rao and co-workers (*Indian Journal of Medical Sciences*, vol. 13, April, 1959) stated that the common method of assessing the quality of human semen is by counting the number of sperms, the percentage motile, and the degree of motility. The estimation of the percentage of motile sperms as carried out routinely is therefore subject to personal error. The authors measured the succinic dehydrogenase content of human semen and tried to correlate it with any of the criteria used in the assessment of the quality of the semen. Over 125 samples of semen from men attending the infertility clinic and a few from donors were studied.

Whole semen, not washed spermatozoa, was used to avoid errors due to centrifuging the samples and washing the sperms. The succinic dehydrogenase activity (SDA) was estimated within two hours after ejaculation. The results showed a close correlation between the SDA and the initial percentage of motile sperms. Azoospermic samples and samples with immotile sperms lacked such activity. The

SDA in other samples varied directly with the initial percentage of motile sperms. This method can be used for quantitative assessment of the initial percentage of motile sperms and is not affected by personal errors. The SDA may have a direct bearing on fertility. That the estimation can be made any time within two or three hours after ejaculation is an additional advantage, when a large number of samples are to be examined.

SWEDEN

Histopathology of the Diseased Gallbladder.—Edlund and Zettergren (*Acta chir. scandinav.* **116**:450-460, 1958/1959) stated that the clinical, surgical, and histopathological terminology of gallstone disease, and particularly of complicating acute cholecystitis, lacked uniformity. They divided a series of 304 patients who underwent cholecystectomy into two main groups, 127 with current or earlier signs of acute inflammation of the gallbladder and 177 in whom such signs were absent.

In the absence of clinical signs of acute inflammation, at the time of operation or earlier, the gallbladder is usually thin-walled and shows a moderate degree of fibrosis combined with round-cell infiltration suggestive of chronic inflammation. Since these lesions are not found in gallbladders not containing stones in elderly persons, and the inflammatory process lacks an initial acute phase, the authors consider the term "primary chronic cholecystitis" appropriate for the thin-walled gallbladders containing stones. The presence of stones is a prerequisite for acute inflammation of the gallbladder. This implies that the gallbladder wall is affected with primary chronic changes prior to the development of the acute cholecystitis. In acute cholecystitis the gallbladder is occluded, in most cases. The usual cause of the occlusion is a so-called obstructive stone. The course of acute cholecystitis follows a fairly fixed cycle of phases to the healing stage, "secondary chronic cholecystitis."

This chain of events may in some instances be disturbed by acute exacerbations. "Acute cholecystitis" should be the diagnosis in patients undergoing operation within seven days of the onset. If the operation is performed in the second week the diagnosis would be "subacute cholecystitis." When the operation is performed in the third or fourth week after the onset, it would be "subchronic cholecystitis," and if the patient undergoes operation in the fifth week after the onset or later, it would be "secondary chronic cholecystitis." If the inflammation shows signs of exacerbation during the stages labeled subchronic cholecystitis to secondary chronic cholecystitis, the diagnosis would be modified by the words "with acute exacerbation." The authors believed their classification of acute cholecystitis to be justified, since it affords a basis for discussion of therapeutic principles. The differentiation of primary and secondary chronic cholecystitis was, in their view, of utmost importance when comparing therapeutic principles and results in different series.

Rupture of the Tendo Calcaneus.—Normally, the tendo calcaneus is one of the strongest in the body. The blood flow in the tendon is decreased after the third decade of life, which may explain the normal occurrence of certain changes in the tendon tissue with rising age. Subcutaneous rupture of the tendo calcaneus cannot, however, be explained only on the grounds of its decreased resistance due to the aging process. Such ruptures are uncommon, and the eliciting violence is often relatively slight. Moreover, the injury is predominant in men and is most common below the fourth decade.

O. Arner and co-workers (*Acta chir. scandinav.* **116**:484-490, 1958/1959) reported a series of 74 subcutaneous ruptures of the free part of the tendo calcaneus in 71 patients. In 71 cases this was the first rupture of the tendon, whereas 3 ruptures had been treated earlier but a fresh rupture had occurred two and one-half to three months after the first one. The 74 ruptures were operated on from a few hours to eight months after they were incurred. At operation parts of the tendon were excised for histological examination. In every case such examination showed the presence of more or less marked characteristic degenerative and necrotic changes. Distinct degenerative changes were found even in the 12 patients in whom operation and biopsy were performed within 24 hours of the rupture. Consequently, the degenerative changes could not be secondary to the traumatic tissue damage. Degenerative changes in the tendon seemed to be a prerequisite for rupture of the free part of the tendon.

Inflammation and regeneration appeared secondarily to the tissue damage and hemorrhage associated with the rupture and were entirely unrelated to the degenerative process. The inflammatory and regenerative changes permitted an approximate histological evaluation of the age of the injury. Four fairly well-defined stages of healing could be distinguished. The histological examination provided no definite information about the cause of the degenerative changes. Hypertrophy of the media, with narrowing of the lumen in medium-caliber vessels, was present in some cases, but no other vascular changes of importance could be observed. No signs of specific inflammation or tumor were present in any specimen. The histological findings seemed to be compatible with the assumption of an impairment of the blood supply as the causative factor.

In another study Arner and co-workers (*Acta chir. scandinav.* **116**:496-500, 1958/1959) described a new roentgenographic sign of rupture of the ten-

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don; namely, a deformity of the contours of the distal segment of the tendon resulting from loss of tone, which they regarded as pathognomonic.

Sacral Anesthesia.—At the second surgical department of the Södersjukhus, in Stockholm, tests with various strengths of lidocaine given for sacral anesthesia have shown that, with a 0.5% solution, 18 to 20 ml. can be given not only to inpatients but also to outpatients. K. L. Wiechel (*Nordisk medicin*, June 4, 1959) came to this conclusion after giving a 1 or 2% solution, which, although it did not provoke any alarming reaction such as cardiac arrest, anoxia, or great fall of blood pressure, had the undesired effect of extending the anesthesia induced beyond the intended limits. The ensuing partial paralysis of the muscles of the lower limbs contraindicated the use of this strength in outpatients in whom lumbar anesthesia has been found unsuitable. With use of 0.5% solution to which a vasoconstrictor had been added Wiechel achieved satisfactory anesthesia in 159 of 160 patients, 45 of whom were outpatients. The operations were on the anus (for polyps, fistulas, hemorrhoids, and tumors) in 62, and on the bladder for such procedures as electroresection in 73. Transvesical prostatectomy was performed in 19. With the risk of paraplegia avoided by this dosage, lidocaine can prove useful for polyclinic practice.

Epilepsy Studies.—C. G. Bernhard (*Nordisk medicin*, June 11, 1959) of the Karolinska Institute in Stockholm found that certain patients react to lidocaine in a way pointing to the possible exploitation of local anesthesia in the treatment of epilepsy. E. Bohm of Stockholm reported in the same issue that, of 36 Jacksonian seizures in 27 patients, 26 were arrested by intravenous injections of lidocaine in doses of 1 to 5 mg. per kilogram of body weight.

Treatment of Depression with Imipramine.—Hanson and Punell (*Svenska Läkartidningen*, May 22, 1959) treated 50 women who had various depressive psychoses with imipramine. Most of them were elderly, 44 being over 50 years of age. The preference shown for older women in the selection of patients for this treatment reflected the unsuitability in many of their cases of shock treatment and other drastic measures. The drug was given orally or intramuscularly in doses of 25 mg. three times daily. This was gradually raised to a maximum of 350 mg. daily. Of the 14 patients with more or less disturbing side-effects treatment had to be discontinued in only 2. The high rate of side-effects, in comparison with those of other observers, may have been due to the relatively advanced age of the patients, hence the advice that the dosage should be regulated according to individual needs and to the increasing dosage of the drug. In roughly 67% of the patients a definite antidepressive effect could be claimed. While the duration of the illness did not seem to affect the reaction to the drug, the side-effects rose in frequency with the patient's age. Relapses were successfully counteracted by resuming administration of the drug, when it had been prematurely discontinued, or by raising the dose when the maintenance dose had been too low. Although there are no absolute contraindications for this treatment, it may be well not to use it in patients with latent or manifest epilepsy or in the presence of advanced arteriosclerosis.

UNITED KINGDOM

Artificial Insemination.—The Council of the British Medical Association (BMA) submitted a memorandum on the medical aspects of artificial insemination to the departmental committee set up by the home office last year to investigate the problem. The BMA council considered that artificial insemination by a donor other than the husband of the woman (AID) does not contravene any of the accepted principles of scientific medicine. Nevertheless many physicians consider the practice undesirable, and are opposed to it on religious and moral grounds. The demand for AID is not large, and in the last 20 years probably no more than 2,000 women have conceived by this method in Britain. Probably fewer than 20 doctors in this country are engaged in the practice of donor insemination.

The council accepted the view that in the hands of skillful practitioners AID may result in satisfaction to the couple concerned and in a healthy child, who could be brought up in circumstances which would not necessarily subject it to psychological trauma. It admitted, however, that harmful results to the marriage and to the child can occur if the couples are not carefully selected or are psychologically unbalanced. Statutory prohibition is undesirable because it might lead to the practice of AID by unskilled and unqualified persons. The procedure involves a minor operation and this, with the selection of suitable couples and donors and their physical and psychological examination, involves knowledge of gynecology, male infertility, psychological medicine, and human genetics. Doctors engaged in this work should therefore have special skill and experience.

The council considered that before proceeding with AID the physician should investigate the motives of the couple and the stability of their marriage; explain the matter carefully to them as well as the alternatives, such as adoption; accept responsibility for the selection of a suitable donor; and obtain written consent from both husband and wife.

The council stated that the success of AID depends on the maintenance of a stable and normal family life for the child. All records of the case should be kept strictly confidential and in a central registry. They should only be available for inspection on the order of the high court.

The council did not recommend any changes in the laws relating to birth registration, whereby the husband is registered as the father, and to a decree of nullity, but it considered that the practice of AID necessitates clarification of the laws dealing with these. While it is not in a position to advise on the legality of the practice of AID, it recommended that it should be illegal for anyone but a medically qualified person to carry out the procedure; that it should be available only to married persons; that the donor should be unknown and unrelated to the couple concerned; that the doctor carrying out AID should not be a donor; and that a confidential register of successful donor inseminations be established.

Printers' Strike.—Owing to a dispute in the printing trade, which has brought 100,000 men out on strike, many periodicals have ceased publication. *The Lancet* solved the difficulty by publication in Germany. Its last three issues, which are much reduced in size, were printed in Bremen. The *British Medical Journal* is being printed by a firm employing non-union labor, but owing to a shortage of ink the print is rather faint. A motion was carried by the Socialist Medical Association, which supports the strikers, describing the printing of the last issue of the *British Medical Journal* as "ill-advised" because non-union labor was employed. It stated that at a time when the British Medical Association was pressing for an increase in the remuneration of the profession, which is just what the printers are doing, such an act was ill-advised as it jeopardized the good will of the labor movement, and without this good will the cause of the medical profession would suffer. Dr. Hugh Clegg, the editor of the *British Medical Journal*, described this motion as "a piece of gross impertinence." Any interruption of the publication of the journal would be an act of sabotage against the health service. He said that he had approached the printers' union to see if the journal could be produced by union labor, but he was not successful. Medical information of value to doctors in treating their patients is being held up by the reduction in size of the journal and the delay in its publication.

Sex Crimes and Mental Patients.—The popular fallacy that sex crimes are usually perpetrated by mentally defective persons was disposed of by the Lord Chancellor, Viscount Kilmuir, in the House of Lords in a discussion on the mental health bill. According to the evidence obtained by a home office research unit, only a small proportion of offenders convicted of sex offenses have a history of treatment for mental disorders. In the last six months of the period in which records were available 3,630 persons were convicted in the courts of England and Wales for such offenses. Only 261, or just over 7%, had received treatment for a mental condition. Of 964 cases of indecent assault on young persons under 15, only 50, or about 5%, of the offenders had a history of mental disorder. The Lord Chancellor said that society would not be justified in detaining indefinitely in mental hospitals patients considered dangerous to themselves or other people simply because they might resort to a comparatively minor form of crime.

Causes of Death.—In the registrar general's report for 1958 for England and Wales deaths from coronary heart disease continued to increase—84,048 compared with 76,324 in 1957 (The Registrar General's Quarterly Return No. 441, 1959, Her Majesty's Stationery Office). Of these, 52,089 were in men and 31,959 in women. There were 19,807 deaths from cancer of the lung, or 690 more than in the previous year, and 17,030 of these deaths were in men. There was a drop in deaths from influenza from 6,716 in 1957, when Asian influenza was at its height, to 2,402. Deaths from bronchitis showed an increase. There were 29,392 deaths, of which 20,326 were in men.

Poliomyelitis deaths, which were 130, were 96 fewer than in 1957. There were record low numbers of deaths from diphtheria (8), scarlet fever (4), whooping cough (27), and smallpox (1). Deaths from traffic accidents were 5,438 against 4,898 in 1957. Neonatal mortality continued to decline from 23.7 deaths per 1,000 live births in 1956 to 22.6 in 1958. The rate was lowest in the eastern counties of England, and highest in Wales. Accidental deaths at 4,623 for the quarter were higher than for the corresponding quarter in 1957. There were 2,381 deaths from accidents in the home, with 175 more than in 1957. There were 358 accidental deaths from carbon monoxide poisoning.

Queen's Birthday Honors.—Several medical men figured in the honors list published on the Queen's birthday. A baronetcy was conferred on Prof. Robert Platt in recognition of his services as President of the Royal College of Physicians, to which he was elected in 1957, and for his encouragement of medical research and education. His own investigations on renal disease have earned him an international reputation. Dr. Wilfred Sheldon, pediatrician at King's College Hospital and the Hospital for Sick Children, London, was made a Knight Commander of the Royal Victorian Order, a distinction which

carries a knighthood, for his services to the royal family. The same distinction was granted to Sir Archibald Gray, a dermatologist and university administrator, who has done much for medical education and the organization of medical schools. Air Vice-marshal F. W. P. Dixon, an Australian who became a distinguished surgeon in the R. A. F., was made a Knight Commander of the Order of the British Empire. Professors Dugald Baird and Aubrey Lewis and Mr. Alexander Gillies became Knights Bachelor. Professor Baird, of Aberdeen, has made numerous investigations on the social and nutritional aspects of childbearing. Professor Lewis, an Australian, directs the professorial unit in psychiatry at the Maudsley Hospital, London, where he has encouraged much research in this field. Mr. Gillies is a consulting surgeon to the Wellington Hospital, New Zealand.

Death of Dr. Grantly Dick-Read.—Dr. Grantly Dick-Read, who died recently in Norfolk, aged 69, was best known for his advocacy of "natural childbirth." Although his principles were basically sound, his views and methods did not always meet with the approval of the profession. He lectured on natural childbirth in Britain, France, and the United States, but with the coming of the National Health Service in 1948, he found that he could not continue his work, because he had never qualified by examination as a gynecologist. He then went to South Africa and practiced in Johannesburg. He later returned to England and devoted his time to lecturing and writing.

Dick-Read's interest in natural childbirth was aroused when as a young doctor in 1914 he started to give chloroform to a woman in labor. She refused it and when the baby was born remarked that she suffered no pain and that presumably she was not meant to. In his book "Natural Childbirth," he stated his belief that labor should be painless and that if pain did occur it arose through fear and tension. His other works were "Revelation of Childbirth" (1943), "Childbirth Without Fear" (1944), "Birth of a Child" (1947), "Introduction to Motherhood" (1950), and "No Time for Fear" (1953).

Prednisone for Insulin-resistant Diabetics.—The demonstration of the presence of substances capable of neutralizing the action of insulin in the serums of insulin-resistant diabetic persons has led to many attempts to discover their nature and etiological significance. Observations made by Oakley and co-workers (*Brit. M. J.* 1:1601, 1959) favor the view that insulin-resistance in man may be produced by an excess of insulin antibodies. The reason for this belief is that prednisone has been shown to cause a rapid and dramatic fall in the insulin requirements of patients in whom it has been possible to demonstrate the presence of antibodies by means of the guinea pig passive cutaneous anaphylaxis (PCA) test. The failure of prednisone to exert this action in two cases in which the PCA test was negative is in keeping with this view. The diabetic patients in whom these results were obtained were highly insulin-resistant, requiring from 200 to nearly 1,500 units of insulin daily. It is difficult to explain the action of prednisone in any other way as it normally increases insulin requirements.

Poliovirus.—Finch and Klug have deduced the structure of the poliovirus from x-ray diffraction studies of the virus crystals (*Nature* 183:1709, 1957). The x-ray photographs show for the first time in a virus investigation that poliovirus has a degree of crystal perfection comparable with that of the lower molecular weight crystalline proteins. The crystal symmetry appears to be icosahedral, which means that it contains 60 structural protein units. If small deviations are ignored each virus particle is surrounded by eight others at a center-to-center distance of 304 Å units. The virus particles are packed in a nearly regular hexagonal array.

The subunits in the poliovirus particle may not be identical since differences of one or two amino acids between the protein molecules in a virus cannot be detected by the x-ray method. The molecular weight appears to be about 6,700,000 and of this 25 to 30% is ribonucleic acid. The molecular weight of the protein part of the molecule is about 80,000. Electron microscopy suggests that the ribonucleic acid is located within the shell formed by the protein. So far, the structure resembles that of the small spherical plant viruses, and it is probably safe to conclude that there are no structural grounds for distinguishing the smaller animal viruses from the plant viruses.

The infectivity of a virus is carried by ribonucleic acid, and the function of the protein part is presumably to provide some form of packaging. The ribonucleic acid controls the formation of virus protein and "codes" the sequence of amino acids. There will be a limit to the lengths of polypeptide chain produced, set by the ribonucleic acid content of the virus, and the virus protein will be constructed from a relatively large number of small protein molecules. This is how the connection with the icosahedral symmetry is accounted for, since of all types of cubic symmetry it allows the greatest possible number, namely 60, of identical structural units in building the framework. The icosahedral symmetry in virus structure is, thus, a matter of economy. It gives the most efficient packing of subunits in a virus particle.

CORRESPONDENCE

DEATH RATES FROM AUTOMOBILE ACCIDENTS

To the Editor:—The letter by John H. Schaefer, M.D., in the June 27 issue of THE JOURNAL concerning Dr. Thorndike's paper published in March deserves some comment. Dr. Schaefer is correct in the figures he uses, but these are not the death rates per 100,000 population universally used in estimating death rates from disease and injury. It is true, as he states, that the death rate per 100 million miles has shown a steady decline over the years, but the true death rate as it affects the American people, which is the death rate per 100,000 population, has shown little change in the last 10 years due to the increased number of vehicles and the increased number of miles traveled on American highways.

The death rates per 100,000 population from automobile accidents as compiled by the National Safety Council for the last 10 years are as follows:

1949	21.3	1954	22.1
1950	23.0	1955	23.4
1951	24.1	1956	23.9
1952	24.3	1957	22.7
1953	24.0	1958	21.4

The declining death rate per 10,000 vehicles and per 100 million miles is viewed favorably by some of the automobile manufacturers who wish to minimize the highway toll in the minds of the public and by the professional safety people who wish to make their work look good.

The most important factor in holding the national death rate where it is is undoubtedly the improvements made in the last few years in surgical technique, the more ready availability of blood for transfusion, and the effect of antibiotics. It is probably impossible to estimate this effect statistically, but I think any of us who have had experience with trauma extending back past the days of blood banks and antibiotics would agree that modern techniques have transferred many of the severely injured from the fatality column into the severely injured but living column.

This view is supported by statistics compiled by the Travelers Insurance Company of Hartford, Conn., which show a 12% increase of injuries in 1958 over 1957, compared with a 5% decrease in deaths for the same period. The following quotation from the Travelers Publication, "The Road Toll" is significant: "In the 20 year period from 1938 to 1957, the annual death toll rose from 32,000 to 38,700, an increase of 20%. At the same time the number of injuries increased from 1,145,000 to 2,525,000, a gain of 120%. During this same 20 year period, motor vehicle registrations increased 128%. Thus the total number of casualties has kept pace with the increase in registrations and the fact that deaths have not risen proportionately is hardly a cause for rejoicing. Many thousands, whose injuries might once have proved fatal, are alive today, only because of the improved medical and surgical techniques of the past 20 years. The total number of casualties rather than the number of deaths should be the yardstick used to measure the degree of success or failure of accident prevention programs."

From the standpoint of loss of productive years to the American public, the accident death rate is probably still the most important public health problem.

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DISCUSSIONS AT BEDSIDE

To the Editor:—Dr. Steinchrohn (*J. A. M. A.* **170**:1458 [July 18] 1959) is correct when he chides us for discussing patients with other physicians at the bedside, often as if the patient were not there, and sometimes surely not to the patient's benefit. He may be interested in a study carried on by two physicians on our psychiatry service which concerned itself with the patient's reaction to bedside teaching (Preuss and Solomon: *New England J. Med.* **259**:520 [Sept. 11] 1958). These observers found an interesting variety of emotional reactions to ward rounds and specifically to discussions at the bedside. The point was made, however, that not all bedside teaching was upsetting to the patient nor need any of it be. In fact, "it was found that these exercises were often of great reassuring value to patients, but that on some occasions ill advised and unnecessary remarks were made that were embarrassing, frightening, and angering."

The thought which might be derived from this study is that ward rounds conducted with full recognition of the patient's presence might well be therapeutic and of positive benefit to the patient as well as being of value in scientific discussions of the problems concerned. Most patients are pleased when a physician and consultants are concerned enough to come to the bedside and discuss their "disease." It might be well for the physician primarily responsible for the patient's care not only to see that bedside discussion is of therapeutic benefit to the patient but also to repair to the patient's bedside after ward rounds to ascertain their effect and thus himself learn of their effect. Because of unpropitious discussions at the bedside, it seems a shame to give up the traditional and still important educational exercise of bedside teaching and consultation. This also is part of the "art of medicine."

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MISCELLANY

MECHANICAL DISEASE INDEXING—A FAST AND EFFICIENT SYSTEM

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and
Sara McKinney, C.R.L., Philadelphia

The Standard Nomenclature of Diseases and Operations, now edited by and published for the American Medical Association, has been accepted throughout the United States as the definitive guide to the nomenclature of disease and of surgical procedures since it first appeared in 1933. It is widely used in hospitals and by doctors as the classification by which indexes are set up. The numerical code numbers assigned to every possible condition or operation make it possible for this to be done in a logical, standard way.

Numerical codes make possible the collection of large quantities of data and the use of such information through punched cards with their high-speed sorting, tabulating, and listing. However, there has been a belief that, because of the detail possible in the Standard Nomenclature, it is not so well suited to such a system as would be a classification with wider, less specific groupings and, therefore, less complicated code numbers—such as the International Statistical Classification. Some who have considered a large-scale operation have been daunted by the fact that the detailed codes for a disease in the Standard Nomenclature of Diseases and Operations may be so long—the number may run to as many as 12 digits for the combination of topography and etiology codes. They feared that, when multiple diagnoses for a single patient needed to be indexed, it would be difficult to get to the material and that cumbersome secondary or trailer cards would be necessary.

One-Card-per-Diagnostic-Entry Method

At the Hospital of the University of Pennsylvania the one-card-per-diagnostic-entry method is used to avoid the handling and rehandling of basic information which must be done under a multiple-diagnoses-per-card method. The "one-per-one" method leads to a collection of data which is flexible, easily translatable into groups of either gross or fine detail, and it provides for cross-indexing without difficulty. No attempt is made to list multiple entries on a single card and there is plenty of space available for the punching of other useful information about the patient and his hospital course. It also means that the over-all occurrence of a disease in the hospital can be found in a single handling of the cards, whether the diagnosis was listed as the primary one or as the second, third, or seventh, in the enumeration of the diseases present. Special punching can show, however, that it was the primary diagnosis, or a secondary diagnosis, or a complication arising after admission.

When proper care has been taken in recording diagnoses precisely and in using all the digits available to express detail, the method will provide with equal ease, for instance, reference to all cases of fracture of the femur, or only to those cases of fractures of the intertrochanteric section of the femur with malunion, or a quick count or analysis of all conditions of the musculoskeletal system due to trauma or physical agent. The immediate accessibility of precisely the information sought is a virtue of modern electronic machines. The virtue of the classification system of the Standard Nomenclature is that the rare, unusual, or seldom-met entity is just as readily available as the larger group to which it belongs.

A drawback to this "one-per-one" method is immediately apparent. There is a greater accumulation of cards than under any other method. This does not mean that the entire bulk of cards must be handled each time information is needed. At the Hospital of the University of Pennsylvania it has been found that by filing the punched cards in numerical order according to the first three digits of the topography code, most demands on the index can be met by handling only a portion of the file. For greater convenience certain sections of the file (for example the 7x.- and 790- groups) may be further subdivided according to etiology. When the entire hospital experience needs to be reviewed, as it does occasionally, the entire file must be handled. This should be contrasted with the need to handle the entire file every time under any other method. It has been found also that the accumulation of cards is not so appalling as had been expected. The cards for certain minor diagnostic entries (but never when they appear as primary diagnoses) and certain minor operative procedures have been withdrawn from the file, printed as listings, and the cards destroyed. If it should ever be necessary, these listings may be translated again into cards for machine handling.

With this done, the inpatient diagnostic and operative experience for nearly six years in this large teaching hospital, where multiple diagnoses and operations per admission are the rule, is on cards which occupy only four 11-drawer double-tray filing cabinets. Of course, an ultimate answer for any unwieldy accumulation of punched cards is its transference to punched paper or magnetic tapes

From the Hospital of the University of Pennsylvania.

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–but experience has proved the present system flexible enough so there is no foreseeable necessity for this transfer.

Some of the details of the "one-per-one" method, as used at the Hospital of the University of Pennsylvania, follow.

When the medical record for an inpatient stay has been completed and the diagnoses are to be added to the index, all the information that is pertinent to such inclusion is abstracted from the medical record and recorded on a code sheet (see figure). Completed code sheets are sent to the tabulating department where each line of diagnosis

Diagnosis code sheet.

and operation information is punched into a single eighty-column IBM card. This is done by means of a "printing punch" in the following manner:

1. All data that need not be translated into a code, such as the six-digit-unit history number, the date of discharge, the age, the number of consultations, and the days stay, are punched as they stand.

2. All other items, except the name, are converted into appropriate codes on the code sheet and are punched as they are recorded.

3. In punching the diagnosis code the structure of the Standard Nomenclature code must be kept in mind. It is basically a two-part six-digit code which may be augmented by adding digits to the right of each set of three numbers. To reflect this flexibility it is important to begin punching the code at the left of the field. Also, because these code numbers may contain decimal digits which electronic machines could not recognize per se, it is necessary to punch any decimal digit as a positional code, i.e., in the last column of the field. The fact that the diagnosis is to be considered as the primary one is indicated by a special punch in another column of the card. With reference to the structure of the Standard Nomenclature code and the need to indicate all decimal digits by position on the card, there are instances when the decimal digit is followed by a qualifying digit or letter. However, because of its relatively infrequent occurrence in diagnoses encountered at this hospital, the digit or letter after the decimal digit of an etiological code is punched in another column of the card.

4. The patient's name is punched into the card. The inclusion of the name may seem to many a useless activity. When the system was designed by one of us (J. P. M.), it was thought that the name was unnecessary so long as the unit history number was used. However, experience has shown that the value of easier recognition of patients by the doctors using the index, and the ability to arrange lists in name order so that correlative lists from other sources (usually identified only by patient name) might the more readily be used, more than compensates for the small additional time needed to punch the name. An additional advantage is that, whenever a number has been transposed or incorrectly entered, the recording of the name ensures access to the case, which would otherwise be lost to the investigator.

Method of Listing Diagnoses

Many examples could be given of ways in which this bank of IBM cards can be used both in large projects and in small ones. The following example illustrates some points. While investigating the relation between hyperparathyroidism and the formation of renal calculi, the tabulating department was called on to sort out all cases in which (*A*) diagnoses of parathyroid tumor (820-8. .) or hyperparathyroidism (820-943.6 and 820-x20) had been recorded and (*B*) a diagnosis of calculi in either kidney or ureter (719-615, 721-615, 722-615 or 723-615) listed. The two groups of cards were matched in the collator, and all cases where the hospital unit number was the same on cards in group *A* and in group *B* were found, and an alphabetical list of these patients was prepared. Alphabetical lists were printed also of those patients in the hyperparathyroid group alone and those appearing only in the renal calculi group. The foundation had thus been

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laid for the compilation of figures regarding the recorded incidence of association of these conditions in one institution, for withdrawal and further study of all three groups of case histories or for follow-up of selected patients. Had several diagnoses been punched on each card, with a possibility of trailer cards in many instances, such collecting of data regarding these associated conditions would have been difficult indeed.

Lists of cases falling into any group may be arranged in any desired order before printing—alphabetical, by age, by date of discharge, by hospital unit history number, by sex, or by color. There are times when no lists of patients are necessary, such as when summaries of incidence are requested for statistical purposes. Often on these occasions the value of collecting all these data in a form that can be processed electronically is most appreciated.

Comment

An attempt has been made to show that the numerical code numbers of the Standard Nomenclature of Diseases and Operations can be used to classify large masses of diagnostic information and attendant details on punched cards in such a way that information can easily be secured whether the items required are seldom-met entities or combinations or gross groupings. It should be emphasized that the results obtained will be only as complete and as reliable as the doctors were in recording the information originally and as others were in translating this into code, transferring it to code sheets, and punching it into cards.

104 Township Line Rd., Llanerch, Havertown, Pa. (Mr. Morris).

A TEST FOR APHASIA

A new diagnostic test for aphasia has been developed by research teams from the University of Chicago and the University of North Carolina. It will be released for general use in November. The test has been under development for the past three years by research groups led by Professors Joseph M. Wepman, of the University of Chicago Speech and Language Clinic, and Lyle V. Jones, of the Psychometric Laboratory at the University of North Carolina. It has been given to more than 200 patients and was designed to determine more specifically than has heretofore been possible the language defect presented by aphasic patients, and thus to permit more effective treatment of the individual problem.

An estimated one million people in the United States suffer, in varying degrees, from aphasia, which is usually caused by strokes and head injuries and occasionally by operations for brain tumor. It occurs most often in persons over 50 years old but may occur at any age. The main instrument in the new test is a metal box which projects simple line drawings and words on a television-like screen measuring 8 by 12 in. The nature of the patient's aphasia is revealed by his degree of ability to name the picture or word, to match the picture with a projected word, to use the word in a sentence, and to respond to the therapist's spoken questions. Specific aphasic defects, such as the inability to use certain areas of vocabulary or to use words in proper grammatical sequence, would be disclosed by the test.

Support for the development of the test came from the U. S. Public Health Service Neurological Diseases and Blindness Study Section and the U. S. Department of Health, Education, and Welfare's Office of Vocational Rehabilitation. Institutions at which the test is currently being demonstrated include the University of Michigan Speech and Language Clinic; Veterans Administration hospitals in Dayton and Cincinnati, Ohio, and Hines, Ill.; University of Wisconsin; Municipal University of Wichita, Kan.; Topeka (Kan.) State Hospital; and Institute for Logopedics, Wichita. Other facilities being visited by the research teams are Veterans Administration hospitals in Pittsburgh and Louisville, Ky.; Walter Reed Army Hospital; and University of Pittsburgh, Speech and Hearing Clinic.

The three basic types of aphasic patients recognized by the research teams are those who (1) are able to speak but cannot summon up the correct words to express their thoughts, and whose words are completely unrelated to the ideas they are trying to discuss, (2) seem unable to form the frequently used connective words of the language, such as "the, and, of," and speak as though they were reading from a telegram, (3) seem capable of using only words of general meaning and speak without specific meaning, as though the listener could supply the important words. Of the patients treated for aphasia about 40% recover sufficiently to return to their previous occupations. Another 40% make some recovery and the rest are not improved. Therapy at the University of Chicago Clinics consists primarily of motivating the patient to practice the use of language. To do this the therapist must often learn to use the terms of the patient's major interest prior to his illness. For example, one of our patients had been a tool and die maker, so in order to motivate the patient to try to talk or write the therapist had to learn the trade talk of tool and die making.

THE LEISURE CORNER

FUN AT THE DRUMS

As the most ancient of musical instruments the drum has served in all ages to express man's love of rhythm. Throughout history it has been a method of communication among less civilized people. The drum has been used for the call to battle, for the requiem for the dead, and as the musical center of ceremonial dances. A great deal of the vitality of contemporary popular music would be lost without the rhythmic beat of the drum.

A drum is constructed of an open cylinder or kettle with a skin known as a drumhead stretched tightly across the opening. When the drumhead is struck sharply it vibrates and produces a sound, which is increased or resonated by the shell of the drum. Drums can be divided into two types, those which have a definite pitch and those, such as the snare drum and the bass drum, which do not. The bass drum is made of wood, with drumheads held in place by metal rods that can be adjusted to increase the resonance. A snare drum, measuring 14 or 15 in. across and from 5 to 10 in. deep, has strings or snares of catgut or wire across the underside. The vibration of these gives the snare drum its characteristic penetrating tone. Among various ethnic groups drums vary widely in shape and in material. Drums can be made of wood, pottery, basket, gourds, coconuts, nutshells, and horns, while drumheads may consist of the skin of deer, moose, buffalo, antelope, tiger, lion, leopard, monkey, elephant, and even man.

Among early American Indians the beating of drums accompanied numerous community functions. This seemed to unite people and develop a feeling of group solidarity and strength. Immediately before battle, for example, lengthy dances were conducted during which the beat of the drum reached an ecstatic pitch, whipping up morale and strengthening the *esprit de corps*. Even today the kettle drums of a band are found psychologically helpful by soldiers, and as for you and me, hearing the drum will often cause us to beat time with our feet.

Whatever it is about the drum that fascinates human beings, it is safe to assume that its rhythmic tonal qualities occupy a most important place. Indeed, there appears to be a universal law of rhythm; we can perceive it in the movement of waves, the rising and falling of tides, the return of night and day and the seasons of the year, and the beating of the human heart. Whenever man senses rhythm he responds to it, even to the point of creating it himself.

It is a familiar fact that sound carries farther on a rainy day than on a clear one. Similarly, the voices of persons on water can be heard distinctly over greater distances than can the voices of those on land. This is the secret of the tones produced by the water drum, for the presence of water within the drum gives sound with far greater carrying power than does a dry drum. Actually, some water drums have been heard 10 miles across a lake. The capacity to be heard great distances distinctly, coupled with its characteristic tonal quality, make the water drum an instrument beloved by those who know it and play it. The Chippewa tribe once regarded the water drum as a medicine drum, possessing therapeutic qualities. In such circumstances, a medicine man would kneel over a sick patient, shake and beat the drum, and incant. Both medicine man and patient firmly believed in the ability of the drum to drive away the evil spirit of illness. As the rhythm of the drum increased, so did the hope of the ailing.

Today, persons who play drums for purposes of entertaining themselves and others find that they are intrigued by shaking rattles and other types of sound-makers. The rhythmic clicking of rattles adds an element of interest and color for the listener. Rhythm sections of dance bands usually feature some rattling device. Dance rattles are of two types, either a hollow shell with a rattle device inside or a rattle device attached to a stick or other object. There is also the gourd rattle, which is widely enjoyed by devotees of such dances as the cha-cha-cha and the rumba. Interestingly enough, this rattle originated among the Indians and played a prominent part in their cultural activities. Of all rattles none is easier to make or more colorful in the production of rhythmic tones. Any dried gourd can serve as a rattle; nothing need be done to it. The neck serves as a convenient handle, and the seeds within strike against the sides, producing a pleasant sound when the gourd is shaken in time. For a staccato sound, however, it is better to clean the pulp from the gourd and add small pebbles on the inside. Finally, drumstick rattles serve a double purpose. These are carried in the hand, providing the drummer within an opportunity to display his skill. Drumstick rattles can produce minute half and quarter beats, which never fail to stimulate a musical group.

Playing the drums puts one in harmony with basic rhythms. Doctors who occupy some of their spare moments with this instrument find it a pleasant form of relaxation. Beating out a rhythm will often unwind tense nerves and add to the zest of living.

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MEDICAL FILM REVIEWS

Surgical Correction of Aphagia Resulting from Bulbar Poliomyelitis: 16 mm., color, sound, showing time 15 minutes. Prepared in 1957 by Benjamin Bofenkamp, M.D., Minneapolis. Procurable on loan from Sister Elizabeth Kenny Foundation, 2400 Foshay Tower, Minneapolis.

The purpose of this film is to demonstrate the author's technique for restoration of the ability to swallow after complete aphagia resulting from bulbar poliomyelitis. The surgical technique is diagrammatically outlined and an actual surgical case is presented. Roentgenograms of the patient's swallowing mechanism, both preoperatively and postoperatively, are also shown. The concept of this film is excellent and its subject matter well organized. Description of pathology and procedure by means of anatomic drawings is excellently executed, and the demonstration of patients before and after operation make this a well-rounded film. However, poor photography of the surgical procedure is very distracting. The over-all views contribute little, and close-ups are taken so low that the surgeon's hands at times obstruct the field. One point was not clear, namely, whether the cricopharyngeus was cut by means of rotating the larynx or actual dissection of the opposite side. This film could be improved by reediting that part dealing with surgical procedure. Although of particular interest to the otolaryngologist this film can also be of value to all physicians.

NEW FILMS ADDED TO A. M. A. MOTION PICTURE LIBRARY

Surgical Repair of Traumatic Interruption of the Ossicular Chain: 16 mm., color, sound, showing time 20 minutes. Prepared in 1958 by George E. Shambaugh, M.D., Eugene L. Derlacki, M.D., and Wiley H. Harrison, M.D., Chicago. Procurable on loan (service charge $4) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film clearly demonstrates three types of injury to the ossicular chain: two caused by former operative procedures and one by trauma. It makes a definite contribution to otological surgery by illustrating some of the injuries which may result in a serious impairment of hearing and which can be rectified. The film depicts at least three methods which can be used, namely, the reduction of a dislocation at the incudostapedial joint, the substitution of a polyethylene prosthesis to provide a columella from the drum to the stapes footplate in a case of a fractured crura and dislocated incus, and the repositioning of the drum to make contact with the head of the stapes in a case in which the incus is no longer available. Both the injury and the method of repair are clearly demonstrated and the photography is excellent. The greatest value of the film consists in the demonstration of different methods by which hearing can be improved by realignment of the sound-conducting mechanism. While this type of injury is not common, the surgical principles demonstrated are used in other types of middle ear surgery. This film is highly recommended for otological surgeons.

Congenital Anomalies of the Ear, Genesis and Correction: 16 mm., color, silent, showing time 37 minutes. Prepared in 1953 by George E. Shambaugh, M.D., and Eugene L. Derlacki, M.D., Chicago. Procurable on loan (service charge $4) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

The embryologic development of the two portions of the hearing mechanism, the sensory labyrinth coming from the ectodermal otocyst and the middle ear sound-conducting apparatus coming from the branchial apparatus, are demonstrated by means of animation. Clinical examples are shown, including one complete operation for congenital meatal atresia. (Reviewed in THE JOURNAL, March 13, 1954, page 940.)

The Effect of Solutions of Different Electrolyte Content on Living Cells: 16 mm., color, silent, showing time 20 minutes. Prepared in 1956 by George E. Shambaugh, M.D., Chicago. Procurable on loan (service charge $4) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

Living epithelial cells from the skin, middle ear, and inner ear were cultured and photographed by phase–contrast time–lapse cinematography. Perfusion of the preparation with normal saline solution, Ringer's solution, and Gey's balanced salt solution was carried out under the camera, showing the relative effects of the various solutions on the living cells. (Reviewed in THE JOURNAL, May 3, 1958, page 104.)

The Fenestration Operation for Otosclerosis: 16 mm., color, silent, showing time 43 minutes. Prepared in 1947 (revised in 1949) by George E. Shambaugh, M.D., Chicago. Procurable on loan (service charge $4) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

The anatomy of the hearing mechanism, with the conduction of sound waves from the outside to the cochlea, is demonstrated. The obstruction to normal sound conduction by otosclerosis is depicted and, by continuing animation, the steps of the fenestration operation to reconstruct a sound-conducting system is traced. An actual operation is shown. (Reviewed in THE JOURNAL, May 29, 1958, page 487.)

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Prognostic Significance of Valvular Involvement in Acute Rheumatic Fever. A. R. Feinstein and R. Di Massa. New England J. Med. **260**:1001-1007 (May 14) 1959 [Boston].

The authors report on 359 patients, between the ages of 5 and 18 years, with an acute attack of rheumatic fever who were hospitalized at the Irvington House prophylaxis clinic in Irvington-on-Hudson, N. Y. These patients had been considered free of rheumatic heart disease before the bout of acute rheumatic fever that resulted in their admission to the clinic. As treatment they received one of 3 antimicrobial agents (sulfadiazine, penicillin, and benzathine penicillin G) to prevent recurrences of streptococcic infections and of rheumatic fever and were examined at monthly intervals. The follow-up period ranged from 2 to 9 years. The patients were classified according to the murmurs present during the acute attack, regardless of what other features of "carditis" might have occurred. The designation "valvulitis" was given to the condition of 129 patients in whom a definite diastolic murmur appeared during the acute attack. The designation "probable valvulitis" was given to that of 52 patients who did not have a diastolic murmur but in whom a loud apical systolic murmur radiating to the axilla or a questionable diastolic murmur or both developed. The designation "no valvulitis" was given to the remaining 178 patients who did not meet these criteria for valvular involvement, although most of this group had other systolic murmurs and many had prolonged P-R intervals, gallop rhythm, cardiac "enlargement," and other features of "rheumatic carditis."

Definite evidence of cardiac enlargement, congestive heart failure, and pericardial friction rub occurred almost exclusively in patients who had valvular involvement. Prolongation of the P-R interval occurred with almost equal frequency in all 3 groups and did not correlate with the subsequent cardiac status. The present figures on the rate of rheumatic heart disease in the 3 groups are as follows: 86 (67%) of the 129 patients with "valvulitis"; 13 (25%) of the 52 patients with "probable valvulitis"; and none of the 178 patients with "no valvulitis." Although additional observations will be needed to confirm these results, the reported data strongly suggest that the auscultatory phenomena present during the acute attack of rheumatic fever are of primary importance in predicting the cardiac prognosis. Patients without "valvulitis" or with "probable valvulitis" may be reasonably assured that subsequent heart disease will not occur as a sequel of the rheumatic attack. These results have obvious clinical and psychological importance in the management of patients with rheumatic fever.

The Clinical Aspect of Tuberculosis After BCG Vaccination. W. Heesen and M.-L. Schwetje. Ztschr. Tuberk. **113**:31-36 (no. 1-2) 1959 (In German) [Leipzig, Germany].

The authors report on 97 patients, between the ages of 1 and 18 years, who had undergone BCG vaccination and who were admitted to the Maria-Grünewald Sanatorium for children and adolescents near Wittlich (Mosel), Germany, between 1950 and 1957 because of suspected active tuberculosis. Of the 97 patients, 5 had received BCG vaccine, although they had had a tuberculous disease before the vaccination; 11 additional patients had unspecific temporary infiltrations; in one child the vaccination remained unsuccessful; and of 2 additional children, one had a mediastinal tumor and the other had pulmonary congestion associated with a cardiac defect. There remained 78 patients, 38 girls and 40 boys, in whom genuine new tuberculosis occurred after the BCG vaccination. In 40 of these 78 patients an intrafamilial source of infection was established. The average age of the 78 patients was 11½ years. The average interval between the BCG vaccination and the first detection of the specific process was 25 months. At the time of the admission of these 78 patients, 3,214 children and adolescents who had not received BCG vaccine were treated for active tuberculosis in the same sanatorium.

Of the 78 patients, 66 were admitted with a diagnosis of postprimary tuberculosis and 12 with a diagnosis of cavitary pulmonary tuberculosis. Of the 66 patients, the diagnosis was confirmed in 61; 33 of these had infiltrations, 9 had pleurisy, 9 had hematogenous dissemination foci, 9 had tubercu-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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lous lymph nodes, and 1 had tuberculous meningitis. The clinical aspect of the tuberculous infection which occurred after the BCG vaccination was benign in all 78 patients, and the clinical course was much more favorable than that in the nonvaccinated patients. Additional tuberculostatic therapy was given to all the patients with postprimary tuberculosis, but the clinical observations showed that the rapid improvement (average 4-month period of treatment as compared with a 7-month period in nonvaccinated patients) was not only the result of therapy but was also due to an increased specific defense condition of the body after successful BCG vaccination. The clinical course was also benign in the patients with cavitary tuberculosis, and the average duration of treatment required was 7 months.

The number of patients with a new tuberculous infection occurring after BCG vaccination has been extremely small, but it still represents a taint. In order to get the statistics right and to prevent a distorted picture of the cases of tuberculosis occurring after BCG vaccination, it is necessary to subject the children to tuberculin tests before the vaccination, to give them careful clinical and roentgenologic examinations, and to determine whether the vaccinated child shows a tuberculin-positive reaction after the vaccination. BCG vaccination of several hundred million persons showed that this vaccination is essentially less dangerous than smallpox vaccination. Despite some not yet fully solved problems, BCG vaccination on a large scale is recommended for persons in certain age groups and of certain professions, and for those particularly exposed to tuberculous infection.

Addison's Disease: Eight Cases: South American Blastomycosis as Possible Etiological Factor in Two Cases. L. M. de Assis, W. Bloise, A. S. Coelho Netto and others. Rev. Assoc. med. brasil. **5**:56-71 (Feb.) 1959 (In Portuguese) [São Paulo].

This study of the clinical, metabolic, and therapeutic aspects in chronic adrenocortical insufficiency (Addison's disease) is based on the cases of 8 patients treated at the Hospital das Clínicas, São Paulo, Brazil. Two of these cases were followed up for 7 years and one for 12 years. Symptoms were typical in all 8 patients, whose ages ranged from 15 to 62 years. Duration of the disease before admission to the hospital's nutritional clinic varied from 1 month to 5½ years. One patient became pregnant in the course of her disease and, on advise of her physician, underwent interruption of pregnancy. Treatment consisted of the administration of either cortisone or desoxycorticosterone (DOCA) or both. Cortisone was given orally in daily doses of 25 mg.; DOCA was given as injections and pellets, with doses varying with the individual. One patient received cortisone only; 4 received both cortisone and DOCA; and 3 received only DOCA. The treatment resulted in normalization of blood pressure, weight gain, and elimination of asthenia in all the patients. One patient died 3½ years after admission to the clinic. In 4 patients the etiological factor could be traced to tuberculosis, which in one case was confirmed at autopsy. In 2 patients bilateral cortical atrophy of unknown origin was suggested.

Two patients in this series presented pulmonary blastomycosis (active in one, inactive in the other), which may have caused destruction of the adrenal parenchyma from the localization there of pathogenic Blastomyces (Paracoccidioides) brasiliensis. This is the first reference in the medical literature to blastomycosis as a possible causal factor in Addison's disease. Based on the association of these 2 diseases in 2 cases, the authors suggest that adrenal lesions in blastomycosis are similar to adrenal lesions in tuberculosis, and they advise that in all cases of blastomycosis a functional investigation of adrenal conditions should be made, even if there are no manifestations of the Addisonian syndrome.

Tobacco Hypoglycemia. M. G. Berry. Ann. Int. Med. **50**:1149-1157 (May) 1959 [Lancaster, Pa.].

Since 1946 the author has seen 24 patients in whom hypoglycemia was produced by the smoking of tobacco. He made the diagnosis of tobacco hypoglycemia only in patients who met the following criteria: (1) use of one or more packages of cigarettes a day (or equivalent); (2) symptoms compatible with the diagnosis of hypoglycemia; (3) blood sugar below 55 mg. per 100 cc. concurrent with symptoms such as nervousness, dizziness, fatigue, "blind staggers," headache, or fainting; (4) prompt relief by the ingestion or administration of glucose at the time symptoms occurred; and (5) complete and permanent relief of symptoms with cessation of smoking. The most important point in the diagnosis is the establishment of a low blood sugar value in the presence of symptoms. Blood withdrawn during an episode of spontaneous symptoms cannot be depended upon. Apparently the lowest levels of blood sugar occur at the onset of symptoms. Many attempts to demonstrate low blood sugar levels in these patients after many hours of fasting were unsuccessful. This may be an important point in differentiating between tobacco hypoglycemia and functioning islet-cell tumor.

Oral glucose tolerance curves, obtained with the use of 100 Gm. of glucose 15 hours after a light evening meal, demonstrated abnormally low blood sugar at the time symptoms were produced in all the patients reported. This method of establishing correlation of symptoms and laboratory confirmation had added value because the patient was under observation. As soon as blood was drawn, glucose could be given when indicated, and its

effect could be noted. The histories of 7 typical cases with tobacco hypoglycemia are presented together with their initial and follow-up glucose tolerance curves. The patients were advised to stop smoking. In every patient who gave up tobacco completely the symptoms subsided, usually simultaneously with the cessation of smoking. In one instance only, the patient required 2 months for complete relief, and it was suspected, but not proved, that the tobacco habit was not immediately conquered. Two patients resumed smoking after abstinence for several months, and in each case the hypoglycemia recurred in about 6 months. Both patients gave up smoking for the second time, after which their symptoms again subsided.

The mechanism by which hypoglycemia can be produced by the use of tobacco is unknown. The incidence of tobacco hypoglycemia in the author's practice was about 0.2%. The condition occurs in individuals who apparently are sensitive to some substance found in tobacco smoke, the most likely being nicotine. Tobacco hypoglycemia is a clinical entity which should be considered in the differential diagnosis of patients with evidence suggestive of either islet-cell hypoglycemia or so-called functional hypoglycemia. Although the great majority of patients with functional hypoglycemia are women, 22 of the 24 cases of tobacco hypoglycemia reported occurred in men.

Heredity in Ankylosing Spondylitis. D. O'Connell. Ann. Int. Med. **50**:1115-1121 (May) 1959 [Lancaster, Pa.].

According to the author, many investigators have estimated that the incidence of ankylosing spondylitis among a patient's immediate relatives is approximately 10%. The data presented in this paper were taken from a study of the relatives of 87 patients with ankylosing spondylitis treated at Charing Cross Hospital, London. A total of 70 families were available for investigation; there were 134 parents, 184 brothers, and 110 sisters, excluding the primary cases. (Only parents and siblings were investigated.) The investigation took the form of a detailed questionnaire to each patient regarding the incidence of disease of the back or hands (ankylosing spondylitis or rheumatoid arthritis) in his family. The patient was then questioned closely about these family members, and arrangements were made for individual examination (including x-ray examination) at Charing Cross or another hospital, or information about the diagnosis was requested from the respective hospital. There were 34 positive answers. These were filtered down to 16 certain or very probable cases of familial ankylosing spondylitis and 7 of rheumatoid arthritis. The author concludes that this series of cases provides supporting evidence for the thesis that there is a strong hereditary factor in the genesis of ankylosing spondylitis (probably a simple dominant with varying sex penetrance). In families in which a female is involved, there is probably an increased likelihood that other members will contract the disease. There appears to be an association in this hereditary factor between ankylosing spondylitis and rheumatoid arthritis.

Acquired Aplastic Anemia: An Analysis of Thirty-Nine Cases and Review of the Pertinent Literature. J. L. Scott, G. E. Cartwright and M. M. Wintrobe. Medicine **38**:119-172 (May) 1959 [Baltimore].

The case records and marrow specimens of all patients with pancytopenia seen at the Salt Lake County General Hospital and the Veterans Administration Hospital in Salt Lake City were reviewed; those secondary to specific marrow disease or the consequence of agents used in the therapy of malignancies were excluded. This report is concerned with the 39 patients who were believed to have acquired aplastic anemia and with a review of the literature. Aplastic anemia is defined as a syndrome in which pancytopenia due to marrow destruction and inhibition is present and evidence of infiltrative disease of the marrow is absent. The acquired form of the disease is differentiated from the congenital aplastic anemia described by Fanconi by the absence of accompanying congenital anomalies and a familial incidence. It affects all age groups and both sexes. Purpura is the most frequent presenting symptom. Minor lymphatic enlargement is sometimes present, but splenomegaly is unusual. There is pancytopenia unaccompanied by morphologic evidence of active cell regeneration. The anemia may be either macrocytic or normocytic. Granulocytopenia may be accompanied by absolute lymphopenia.

Bone marrow sections taken at autopsy or by surgical biopsy usually show reduced general cellularity, but variations ranging from total aplasia to apparent hyperplasia in the same section or in specimens taken from different marrow sites may be observed. Foci of apparent hyperplasia composed only of small lymphocytes are frequently present. Marrow obtained by needle aspiration more consistently shows reduced cellularity than that obtained by biopsy or at autopsy. A percentage increase in morphologically normal small lymphocytes is often found in smear preparations. Ferrokinetic studies show a delayed clearance of isotopic iron from the plasma, decreased in vivo marrow uptake, and a reduction in the percentage incorporation of tagged iron into the red blood cells. Much of the injected iron is incorporated by the liver.

Chloramphenicol was considered to be a probable causative agent of the aplastic anemia in 5 of the 39 patients studied, Mesantoin in 3, and benzene in 2; single cases were probably due to ace-

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tarsone and a sulfonamide. Stoddard's solvent, a petroleum product, may have been the cause of the marrow depression in 4 cases. Three cases followed exposure to agents previously not associated with marrow depression, and 3 followed exposure to more than one potentially etiological agent. The literature on the etiology of aplastic anemia shows the continuing importance of chloramphenicol.

Corticosteroid therapy may occasionally be of benefit in patients with aplastic anemia. Two of 24 patients receiving adequate steroid therapy improved significantly, as manifested by the early development of reticulocytosis and a subsequent reduced or absent need for transfusions. If a trial of corticosteroid therapy produces no benefit, it should be terminated because of the danger of serious infection during prolonged treatment. With regard to splenectomy, the authors say that in 5 of 15 patients operated on transfusion requirements were substantially reduced after operation. Greater longevity of patients who had undergone splenectomy could not clearly be attributed to the operation, but may have resulted from selection for operation of patients with a more favorable prognosis.

Partial or complete hematological recovery was observed in 14 of the 39 patients. The duration of the illness in patients eventually recovering ranged from 3 months to 10 years. Recovery was usually a gradual process. Twenty-one patients died of the complications of prolonged pancytopenia. Hemorrhage, particularly intracranial bleeding, was the commonest principal cause of death. The marrow destruction and mitotic inhibition observed in acquired aplastic anemia are considered to be either the result of an autoimmune process in which various chemicals behave as haptens or the consequence of the direct toxic effects of such agents upon the hemopoietic cells.

A Comparison of Hematological and Clinical Examinations in Patients with Congenital Hemolytic Icterus Before and After Splenectomy. J. Weinreich and H. Schubothe. Klin. Wchnschr. 37:438-442 (April 15) 1959 (In German) [Berlin].

Splenectomy may have a long-lasting beneficial effect on patients with congenital hemolytic jaundice (hereditary spherocytosis). The authors report the results of clinical and hematological studies carried out before and after splenectomy on 10 female patients, between the ages of 10 and 50 years, and on 11 male patients, between the ages of 6 and 28 years, with congenital hemolytic jaundice. The patients were followed up for from 4 weeks to 5 years after the operation. The preoperative findings revealed characteristic changes typical of this disease, but a comparison of the cases studied showed a considerable dissociation of the hematological data. No conclusions could be drawn from the data as to the degree of the severity of the disease. The reticulocyte counts and the serum bilirubin levels in particular did not permit any quantitative conclusions concerning the degree of the increase of the destruction and formation of the blood, nor did the subjective complaints of the patients correspond with the pathological hemolysis. The preoperative serum iron levels showed a definite increase in only some cases. Findings in the patients studied after splenectomy revealed that the blood volume had been restored to normal in some cases and that there was an increase in the erythrocyte count up to its normal range in all patients; however, there was a considerable variation in the values among the different cases (3.9 million to 6.3 million per cubic millimeter). The reticulocyte and bilirubin values decreased accordingly, but remained slightly increased.

Splenectomy resulted in considerable well-being in all the patients studied, including those in whom no anemia was present before the operation and who presumably felt well. It is thus concluded that splenectomy should be performed on patients with hereditary spherocytosis despite the fact that the pathologic increase in blood destruction and formation is only slight. Patients in whom nonspherocytic hereditary hemolytic anemia is present should not be subjected to splenectomy. The differential diagnosis between nonspherocytic and spherocytic hereditary hemolytic anemia must, therefore, be taken into consideration.

Gout and Blood Dyscrasias. J. H. Talbott. Medicine 38:173-205 (May) 1959 [Baltimore].

During the past 25 years the author followed a number of patients who had one of a variety of hematological disturbances. These patients were studied originally because of bouts of acute gouty distress. Some suffered as much from joint symptoms as from the clinical manifestations of the hematological disorder, but the problem in the majority of them was the management of the basic hemopoietic dyscrasia. Twenty-one cases constitute this group.

During the past 5 years the author also made a study of the postmortem protocols of 153 patients with gout. These records were obtained from various hospitals in the United States. While the majority of cases were typical familial gout, 18 cases of clinical gout were associated with a blood disorder. In this group of 153 postmortem protocols there were 15 additional patients who were afflicted with what was familial gout and who died, either because of malignancy, or a malignancy was detected prior to death or at postmortem examination but was not primarily responsible for the death of the patient. The data from patients with nonhematological malignancies were used for comparative purposes. Data on patients with blood dyscrasias

and gout from the author's series and from the postmortem series are tabulated; case histories of some of the author's patients are presented; and reference is made to cases reported in the literature.

There is evidence that polycythemia vera is probably the blood disturbance most frequently associated with clinical gouty arthritis. Myelogenous leukemia appears in the course of polycythemia in some instances and may be responsible for death. There is another variant of polycythemia, namely, polycythemia secondary to a cardiac or pulmonary disturbance, which is responsible for arterial anoxia and may be associated with clinical gouty arthritis. Other blood dyscrasias observed in association with gout are leukemia, myeloid metaplasia, multiple myeloma, pernicious anemia, nontropical sprue, sickle-cell disease, thalassemia (Cooley's hereditary leptocytosis), hemolytic anemias, lead intoxication, Waldenström's hyperproteinemia, and lymphoblastoma. Gout secondary to a blood dyscrasia accounts for approximately 10% of all patients afflicted with clinical gout. In addition, an occasional patient afflicted with familial gout will contract a blood dyscrasia. The concentration of serum uric acid in patients with clinical gout and an associated blood dyscrasia tends to be higher than is observed in familial gout. The author believes that the incidence of malignancy or blood dyscrasias among patients with gout is not connected with colchicine therapy.

The Electroencephalogram in Myxoedema Coma: Clinical and Electroencephalographic Study of Three Cases. E. A. Nieman. Brit. M. J. 1:1204-1208 (May 9) 1959 [London].

That myxedema might be other than an easily remediable condition was largely ignored until recent reports made it clear that coma in myxedema is not a rarity and that it is almost invariably fatal. About 20 cases of myxedema coma have been reported during the past 4 years in Britain alone, and all except one of these were fatal. The clinical picture of coma in patients with myxedema is in many respects similar to coma in hypopituitarism, and it is suggested that some degree of pituitary failure may be involved. The author was able to find only one other report on electroencephalographic changes in myxedema coma, but he was able to obtain electroencephalographic tracings of 2 patients in myxedema coma and of a third patient during recovery from the same condition. They illustrate 3 phases of the same process and the accompanying changes in cerebral electrical activity.

The first of the 3 patients, a 62-year-old woman, was admitted in coma. Her rectal temperature was only 76 F (24.5 C). She had the typical myxedematous facies with coarse, dry, ice-cold skin. Her encephalographic tracing indicated that cerebral electrical activity was reduced to a minimum, although it does not follow that any permanent brain damage would have ensued had recovery taken place. The second case illustrates myxedema coma at an earlier stage, when recovery was possible with the use of thyroid extract, a rather slow-acting agent. In this 45-year-old woman focal neurological signs were absent. The gradual response to thyroid extract was accompanied by electroencephalographic improvement. It is suggested that, had the condition been allowed to progress further, a more rapid agent, such as thyroxin or triiodothyronine, would have been required, and if treatment had been further delayed, no response to treatment might be forthcoming. An intermediate stage in which more rapid and energetic treatment may yet produce a response is exemplified by the third patient, a 70-year-old woman. When she was admitted in coma, her rectal temperature was 87 F (30.6 C). She was treated initially by means of a heat cradle, and triiodothyronine was given by Ryle's tube. There was little change in the first 24 hours, but by 48 hours she was less drowsy, and her rectal temperature was 99 F (37.2 C). Treatment was continued with triiodothyronine, but later this drug had to be withdrawn. The patient died suddenly, and autopsy revealed that death was due to thrombosis of the right coronary artery. The electroencephalogram taken during recovery from coma resembled the records seen in untreated myxedema of moderate severity in the waking state.

It is probable that hypothermia, which is a constant feature of myxedema coma, and deficiency of thyroid hormone itself are the most important factors, though precipitating factors may include environmental cold, trauma, and dehydration. In advanced myxedema coma the tissues may become unresponsive to thyroid hormone, and the condition may be irreversible. Extreme reduction or absence of cerebral electrical activity may indicate this state of affairs and a poor prognosis.

Value of the Voice in Diagnosis of Myxoedema in the Elderly. W. H. Lloyd. Brit. M. J. 1:1208-1211 (May 9) 1959 [London].

Myxedema is apt to be overlooked as a cause of symptoms in those over 60 years of age, if only for the fact that so many in this age group ascribe the symptoms to their advancing years and regard them as inevitable. Most people over 60 attending as hospital outpatients will, on questioning, admit to some symptoms commonly associated with myxedema. These are increasing weight, constipation, falling hair, sensitivity to cold, dry skin, difficulty in walking, vague limb pains, failing of memory and concentration, slow thought, and dizzy spells. Patients with myxedema respond very well to adequate treatment with thyroid. This, coupled with

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the fact that untreated patients with myxedema are unusually prone to death from infection and coma, makes early diagnosis important. The author emphasizes a change in the voice as an important sign. He observed 22 patients with myxedema in the course of 15 months, and in 5 of these the change in the voice was for him the only striking sign of myxedema. The voice changes may take the form of alteration in quality or in diction. The main changes in quality are low pitch, increasing catarrhal or nasal quality, dysarthria with a clotted vocal quality, huskiness, and harshness. With regard to alteration in diction, the author points out that many patients with myxedema speak slowly and deliberately and often have difficulty with certain words, which are stumbled over and slurred. Some, however, speak rapidly and in doing so are unable to retain the normal word spacing, so that slurring of groups of words occurs. Any patient with myxedema may exhibit one or more of these characteristic changes.

The histories of the aforementioned 5 patients are presented; all were over 60 years of age. The diagnosis of myxedema was suggested by the voice. The fact that the voice rather than the facial change was appreciated in these cases suggests that the voice change in myxedema may be pathognomonic. Verbal description cannot adequately demonstrate these vocal changes, but once they are appreciated, they are readily recognized. The author suggests that serial voice recordings can take their place beside serial basal metabolism records and photographs as diagnostic aids in doubtful cases of myxedema.

Calcified Aortic Stenosis. N. Botelho Reis. Rev. brasil. med. **16**:250-263 (April) 1959 (In Portuguese) [Rio de Janeiro].

Detection of valvular calcification in aortic stenosis is of great importance in connection with indications or contraindications for surgical treatment. The clinical manifestations and the course of aortic calcified stenosis were studied by the author in 27 patients in the cardiology department of the Instituto de Aposentadoria e Pensões Brasileiro, in Rio de Janeiro. There were 18 men and 9 women, with ages ranging from 31 to 84 years; the largest concentration (17) was in the 50-to-84-year bracket. The detection of aortic valve calcification was established by radioscopic examination. The criterion for diagnosing calcified aortic stenosis included the presence, besides aortic valvular calcification, of a systolic murmur associated with a symptom or symptoms of aortic stenosis, namely, coronary or cardiac insufficiency, syncope, and fainting. Sixteen patients in the author's series had simple stenosis, whereas 11 presented also aortic insufficiency and 2, mitral calcification. Other complications were coronary calcification in 7 patients, pulmonary emphysema in 6, and diabetes in 2. Clinical manifestations of acute coronary insufficiency occurred in 10 cases, syncope in 4, and fainting in 7. Radiologic findings were normal cardiac area, left ventricular hypertrophy, and dilatation of the ascending aorta. The electrocardiograms showed left ventricular load in 18 patients (diastolic in 8 and systolic in 10). There was a history of rheumatic fever in only 8 patients.

The course of calcified aortic stenosis is linked with myocardial function, depending on the causal factor, degree of stenosis, tendency to valvular obstruction, and complications. Calcification takes a slow course; in 7 of the author's patients there was an interval of approximately 18 years between initial diagnosis of cardiopathy and valvular calcification. Seven patients died within an interval of 3 months to 12 years from the onset. The average duration in this group was 4 years. The causes of death were congestive heart failure in 1, heart failure with angina in 2, coronary insufficiency with angina (sudden death) in 2, subendocardial ischemia in 1, and bacterial endocarditis in 1. The author calls attention to the aggravation of symptoms as signs of the terminal stage and suggests that rheumatic disease and atherosclerosis are the causative factors in calcified aortic stenosis.

Virtue of Prompt Anticoagulant Therapy in Impending Myocardial Infarction: Experiences with 318 Patients During a 10-Year Period. E. S. Nichol, W. C. Phillips and G. G. Casten. Ann. Int. Med. **50**:1158-1173 (May) 1959 [Lancaster, Pa.].

On the basis of observations over a period of years, the authors distinguish the following clinical patterns in coronary atherosclerosis: 1. Patients with no previous signs of coronary disease in whom angina pectoris develops with or without detectable trigger factors, such as smoking, dietary excess, gallbladder disease, hiatal hernia, or emotional stress. Some of this group go along for years without obvious progression of their coronary disease, with intermittent pain controlled by avoiding trigger mechanisms, restriction of activities, and the use of sedatives, ataractic agents, and coronary dilators. 2. Patients with no previous signs of coronary disease, as well as patients from group 1 in whom transmural or subendocardial myocardial infarction develops without warning. The acute attack may prove fatal, or may be followed for a variable interval by angina pectoris or congestive heart failure or an indefinite period free of any cardiac complaint. 3. Patients who manifest the preinfarction syndrome, with or without earlier signs of coronary atherosclerosis or myocardial infarction. The prompt use of heparin and orally given anticoagulants to forestall myocardial infarction in such pa-

tients was the main concern of the studies reported in this paper. 4. Patients from any of the above groups who may develop ventricular fibrillation or cardiac standstill and die suddenly.

The authors evaluate results obtained in a previously reported series and in 141 subsequent cases comprising 318 private patients who were given anticoagulants during the last 10 years because of signs of impending myocardial infarction. Patients were put at rest at home or in hospital, and the usual coronary dilators, tranquilizing agents, and sedatives were used. Heparin administration was begun and was continued for from 3 to 14 days before shifting to orally given anticoagulants. Two hundred sixteen patients had experienced one or more previous attacks of myocardial infarction, while 89 had never suffered an attack, and in 13 it was impossible to determine whether previous attacks had taken place. New electrocardiographic or clinical signs of myocardial ischemia or focal myocardial necrosis were either present initially or developed later in 143 patients (or 44.9%). The diagnosis was based solely on the patient's story in 154 cases (or 48.4%). Frank myocardial infarction developed in 21 patients (or 6.6%), 5 of whom died within a month. None of the others died while using anticoagulants within 60 days of observation. Of 30 patients abandoning anticoagulants before 60 days, 17 experienced "an acute coronary attack" within the next 60 days, with 12 deaths in the following 2 months. Two hundred eighty patients were sustained on long-term anticoagulant therapy indefinitely, but in the intervening years 88 more patients died, mainly of cardiovascular disease, many having abandoned the anticoagulant regimen. Comparable controls are not provided in this study, but the prophylactic benefit of prompt heparin therapy followed by oral anticoagulant therapy in patients showing signs of threatened myocardial infarction appears to be clearly demonstrated. The relief of anginal pain with heparin was often striking.

Mediastinal Syndrome. E. Escobar and H. Ruiz. Rev. méd. Chile **87**:244-252 (April) 1959 (In Spanish) [Santiago].

The mediastinal syndrome is a clinical picture in which the pathology of a mediastinal organ is reflected in an adjacent organ or organs, causing displacement, compression, or irritation. The authors report on 20 adult patients, 8 of whom were treated by them at the Hospital San Borja in Santiago, Chile, between March and August, 1958; the other 12 cases were taken from records of patients treated at the same hospital between June, 1948, and June, 1958. Because there was no classification relating to the mediastinal syndrome as such, the authors studied the records of patients suffering from diseases most likely to be associated with this syndrome and collected data on a series of 198 patients. This series included 118 patients with esophageal cancer, 16 with aortic aneurysms (of which 68.7% were syphilitic and 12.5%, syphilitic-sclerotic), 43 with bronchopulmonary cancer, 6 with chronic lymphoblastic leukemia, and 15 with lymphomas. The clinical picture of the mediastinal syndrome was found to be associated with 9 of the aortic aneurysms, 8 of the bronchopulmonary cancers, and 2 of the lymphomas. The 20th patient in the series suffered from nonaneurysmal aortic dilatation.

The principal etiological factors were aortic aneurysm (45%) and bronchopulmonary cancer (40%). The mediastinal organs most frequently involved included the esophagus in 15 patients (75%) and the trachea in 12 (60%). Other structures involved included the inferior laryngeal nerve, the superior vena cava, the left brachiocephalic venous trunk, the phrenic nerve, the left subclavian artery, and the stellate ganglion. Involvement of nervous structures was associated with bronchopulmonary cancer. The only 2 cases in which the subclavian artery was involved were associated with aortic aneurysm.

The small number of cases found at the Hospital San Borja in a period of 10 years points to the infrequency of the mediastinal syndrome. Radiologic study still constitutes the main diagnostic aid, especially since the development of phleboangiography. Therapy varies with the cause of the syndrome, and the cause varies with the patient's age. Because of the present advances in thoracic surgery, surgical therapy and exploratory intervention tend to be used more and more frequently in dealing with the problem of the mediastinal syndrome.

Studies of Blood Coagulation and Fibrinolysis in Patients with Idiopathic Hyperlipemia and Primary Hypercholesteremia Before and After a Fatty Meal. S. I. Nitzberg, M. A. Peyman, R. Goldstein and S. Proger. Circulation **19**:676-690 (May) 1959 [New York].

The clotting and fibrinolytic activities of the blood were studied before and after a fatty meal in 9 patients with idiopathic hyperlipemia, 10 patients with primary hypercholesteremia, and 10 normal subjects. Six of the patients had evidence of coronary heart disease. Studies were performed to correlate the coagulation and fibrinolysis values with changes in the various serum lipid levels. The results of the coagulation studies were divided into 2 categories. The first was composed of the data obtained by measuring specific coagulation factors. The values obtained for these factors were within normal limits before and after the fatty meal in the 3 groups of subjects. The second category comprised the results of those procedures that measure the over-all coagulability of the blood (or plasma) with or without the addition of thromboplastic material. The results of all these determinations, with

the exception of the thromboplastin generation test and the Stypven time, were within normal limits in the fasting state and remained essentially unchanged after the fatty meal in the 3 groups of subjects. The thromboplastin generation test gave essentially inconclusive results, although there appeared to be a tendency for the hyperlipemic and hypercholesteremic groups to develop a more potent thromboplastin in the fasting state.

The Stypven time (Russell viper venom test) was the one coagulation test that almost always showed significant changes in the presence of hyperlipemia. Thus, it was accelerated (i. e., shortened) in the fasting state in all the patients with idiopathic hyperlipemia. In addition, the Stypven time was accelerated in all groups of subjects after the fatty meal. Comparison of these results with the serum lipid levels showed that there was some correlation between the Stypven time values and the serum triglyceride levels (and the fatty acid levels to a lesser extent), as well as with the turbidity of the serum in all groups of subjects before and after the fatty meal. No correlation was found between the Stypven time and the serum cholesterol or phospholipid levels. Two methods were employed to assess the fibrinolytic activity of the blood. Method 1, which measured blood fibrinolysis directly, gave variable and inconclusive results. Method 2, which determined the fibrinolytic activity of plasma after activation with streptokinase (in vitro), showed that prolonged streptokinase fibrinolysis times occurred under circumstances similar to those associated with accelerated Stypven times. Thus, there appeared to be an association of the fibrinolysis time with the serum triglyceride levels as well as with the serum turbidity. The behavior of the blood clotting and fibrinolytic systems in the 6 patients in this series who had evidence of coronary artery disease did not differ from that of the other individuals within the same groups either in the fasting state or after the fatty meal. Further studies are necessary for a final elucidation of the exact relationship between the serum lipids and the coagulability of the blood, and its possible connection with coronary artery disease.

Plasma Catechol Amine Concentrations in Myocardial Infarction and Angina Pectoris. P. C. Gazes, J. A. Richardson and E. F. Woods. Circulation **19**:657-661 (May) 1959 [New York].

There have been reports that the adrenergic catechol amines (epinephrine and arterenol [norepinephrine]) cause a wastage of oxygen by the heart muscle. On the other hand, a "stress-adapting mechanism" has been ascribed to the catechol amines, which seems to make the heart more efficient in the utilization of oxygen. In either event an excess of these amines may be of clinical significance in patients with myocardial infarction or angina pectoris. Studies were performed to correlate plasma catechol amine levels in patients with myocardial infarction and in those with angina pectoris. Arterenol plasma levels were significantly increased in 13 patients with myocardial infarction, and in 7 of these there was also a significant increase of epinephrine, as compared with 7 normal subjects. There were no comparable increments of the amines in 6 patients with noncardiac type of pain. In 7 patients with myocardial infarction, there was a positive correlation of arterenol and transaminase levels, but there was no such relationship with epinephrine and transaminase. In 12 patients with angina pectoris, the level of arterenol increased in 8 after exercise, whereas epinephrine increased in only 5. There was no significant change with exercise in the 7 normal subjects. It is believed that these increases in plasma catechol amines in patients with myocardial infarction and angina pectoris may play a significant part in therapy and prognosis.

Sudden unexpected cardiac deaths from ventricular fibrillation have been observed in patients in whom autopsy revealed various degrees of coronary sclerosis but no significant myocardial lesion. Anoxia with accumulation of lactic acid may be associated with stimulation of chromaffin tissue within the heart and release of epinephrine and arterenol. This is a possible mechanism, since lactic acid is a potent stimulant to the chromaffin tissue of the adrenal medulla. Since there is reason to believe that these amines intensify the anginal pain in patients with coronary sclerosis, a reduction of circulating amines or a blockade of their effects appears as another rational therapeutic approach to angina pectoris.

The most practical method is that of physical rest and mental relaxation to diminish sympathetic stimulation. Exposure to cold temperatures, heavy meals, and excessive tobacco smoking should likewise be avoided, since they can be expected to cause increased discharges. Thoracic sympathetic ganglionic block or sympathectomy and sympatholytic drugs have been used with encouraging results. Roentgen irradiation of the adrenal glands and later total ablation of the thyroid by drugs, surgery, or radioiodine (I^{131}) have also been utilized. Thyroid hormones intensify the adrenergic action on the heart. Although glyceryl trinitrate (nitroglycerin) may have a specific antiadrenergic action on the heart muscle, in addition to its coronary dilator effect, it more probably acts largely by reducing peripheral resistance and thus reducing the work load of the heart. Acute stimulation of the vagus by pressure on the carotid sinus has been recommended to terminate anginal attacks with occasional striking results. It initiates an antiadrenergic, oxygen-sparing effect upon the myocardial metabolism.

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Papilloma of the Esophagus: Association with Hiatal Hernia. R. H. Adler, D. M. Carberry and C. A. Ross. J. Thoracic Surg. 37:625-635 (May) 1959 [St. Louis].

Recent experience with a patient having a localized sessile tumor in the distal esophagus, which was diagnosed histologically as papilloma, stimulated the interest of the authors in this subject and prompted a review of their own records and of the available literature. This is apparently the first documented case of papilloma of the esophagus associated with hiatal hernia and distal esophageal stenosis. As far as the authors know, it is also the first case in which thoracotomy was performed with resection of the tumor and the involved esophagus. The patient, a 73-year-old man, recovered. A soft papillary nodule with a broad base was noted on the mucosal surface of the resected esophagus. It measured approximately 0.8 cm. in diameter and projected about 0.3 cm. into the lumen. In close proximity to the papillary lesion, a 0.4-cm. ulcer, probably representing the site of a previous biopsy, could be seen. Microscopic study on the sections revealed a papillary lesion with vascular fronds of connective tissue covered by well-differentiated squamous epithelium. Parakeratosis and hyperkeratosis were present in the papillary projection. There was no evidence of invasion into the broad pedicle. These sections are interpreted as a papilloma of the esophagus because of the true formation of papillary projections rather than artifactial folds.

On reviewing their clinical material of the 11-year period from January, 1947, to December, 1957, the authors found 205 cases of carcinoma of the esophagus. In 4 of them esophagoscopic biopsies performed proximal to the malignancy revealed papilloma of the esophagus, but this diagnosis was not upheld when the material was reexamined at the time of this review. These 4 cases are briefly described. There was esophageal obstruction due to malignancy in all of them. After reexamining the original histological sections and reviewing the clinical data, it was apparent that the mucosal lesions were areas of mucosal hyperplasia and papillary folding rather than true esophageal papillomas. With such lesions, particularly, papilloma of the esophagus has been confused.

The significance of papilloma of the esophagus remains unsettled. Of first importance is the danger that a diagnosis of papilloma based on esophagoscopic biopsy may divert attention from a more distal esophageal lesion that may be an unsuspected carcinoma. The papilloma itself has been considered to be a benign tumor that needs attention in only the rare case when it causes symptoms. Papilloma should not be confused with granulomatous proliferations and sessile glandular polyps. A papilloma may be readily differentiated from leukoplakia with its features of hyperkeratosis and epithelial atypism. Nevertheless, one cannot be absolutely certain that esophageal papilloma does not represent merely an advanced stage of localized epithelial hyperplasia or mucosal proliferation. The dividing lines between certain of these proliferating mucosal lesions may be vague in some cases, and absolute definitions demand, at best, complete gross and histological examination of the growth and the adjacent esophagus. Perhaps as more attention is directed to the lower esophagus by clinicians and pathologists, the true nature of papilloma and related sessile mucosal lesions may become better understood.

The Value of Bronchoscopy in Determining the Inoperability of Carcinoma in the Lung. E. B. Benedict. J. Thoracic Surg. 37:646-650 (May) 1959 [St. Louis].

While bronchoscopy is widely recognized as an important factor in the diagnosis of bronchial carcinoma, it is not so well established that it can give information regarding the resectability of the lesion. The author emphasizes that a physician who only occasionally performs a bronchoscopy is generally not competent to estimate operability, as this requires wide experience. The following points are of special importance: If a lesion involves the trachea, the chance of successful resection is slight. Widening and fixation of the carina usually mean that the tumor has invaded the mediastinal glands to such an extent that it cannot be removed. If the bronchus is fixed in the region of the carcinoma, it often means peribronchial invasion of such a degree as to mean unresectability. Extrinsic pressure frequently causes abnormal angulation of the bronchus probably due to metastatic glands or local extension of the growth, making resectability unlikely. Narrowing of the bronchus may mean infiltration of its wall by carcinoma or extrinsic pressure from local extension of the tumor or from metastases in lymph nodes. If this is accompanied by fixation, resectability is unlikely.

In reviewing a series of 3,247 bronchoscopies, the author found 147 cases of proved bronchogenic carcinoma which he thought were probably inoperable. In 120 of the 147 patients (81.6%), the bronchoscopic studies plus the physical and x-ray findings were so unfavorable that surgery was not done. In 17 other cases (11.6%), the bronchoscopic report was unfavorable, but exploratory thoracotomy was performed anyway, and the tumor proved to be unresectable. In 8 cases (5.5%), resection was possible in spite of the unfavorable bronchoscopic report; however, the surgical result was poor both as regards palliation and length of survival. In the remaining 2 cases (1.4%), the bronchoscopist's judgment was incorrect, and the tumor was resected with good result.

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Emergency Pulmonary Resection in Necrotizing Pneumonia. T. H. Hewlett, L. M. Bitner and P. Moraca. J. Thoracic Surg. 37:580-597 (May) 1959 [St. Louis].

The fact that epidemic influenza may set the stage for staphylococcic pneumonia is well established; however, it can no longer be considered the sole predisposing factor. Minor upper respiratory infection of an acute nature may pave the way for staphylococcic invasion of the bronchopulmonary tree. Chronic bronchitis and pulmonary edema may establish a favorable environment for the growth of staphylococci in the respiratory tree. A fatal staphylococcic process may develop as a superimposed infection in sites altered by pneumococcic pneumonia. Mortality rates vary in these different forms of staphylococcic pneumonia, ranging from 15% in the abscess form that can be expected to drain via bronchial routes to 80 or 90% in acute necrotizing pneumonia. The authors describe the initial effect of Staphylococcus aureus on pulmonary tissue, and discuss the various pictures established by the infection in the lungs of infants and of adults. Drainage is an essential feature in the types of disease that exhibit a tendency to recover on conservative management. Necrotizing pneumonia is still an unsolved problem. The histories of 4 patients are presented, in whom emergency pulmonary resection was carried out during the acute phase of necrotizing pneumonia.

The first patient, a 41-year-old army nurse, had been treating herself for a cold for approximately 3 weeks with antipyretics and orally administered antibiotics. Ten days prior to admission, pharyngitis and rhinorrhea had become marked. A throat culture yielded Diplococcus pneumoniae. X-ray studies showed infiltration limited to the middle lobe of the right lung. The therapeutic regimen instituted on admission consisted of daily doses of 40 million units of penicillin, 2 Gm. of streptomycin, and 2 Gm. of Achromycin. Isoproterenol (Isuprel) was given every 2 hours, and positive pressure was applied intermittently. Postural drainage of the middle lobe was attempted. The patient showed no response to a 10-day course of this treatment. Repeated aspiration via the bronchoscope was ineffective. Throughout the hospital course, the roentgenograms revealed persistence of the middle lobe consolidation. On the 23rd day an emergency middle lobectomy was carried out. The prompt clinical response to lobectomy in this patient indicated that emergency resection might be useful in the management of certain acute pulmonary infections which did not drain via normal routes and which did not improve on adequate medical therapy.

In the second patient a left-sided pneumonectomy was performed on the 70th day of the disease. This patient died, but in retrospect it seems likely that he would have survived if thoracotomy had been carried out when it was first proposed. Desperation pneumonectomy in the face of contralateral disease is not advocated. In the third patient, in whom necrosis involved only the lower lobe of the right lung, recovery resulted from lobectomy. Lower lobectomy on the left side controlled the acute process in the fourth patient.

The development of antimicrobials has not obviated the need for drainage in staphylococcic infections. In necrotizing pneumonia effective drainage does not occur for several reasons. Normal ciliary reflexes of the bronchial mucosa are lost because of widespread destruction in the bronchial wall. The gelatinous necrotic debris that collects in the bronchi serves as a mechanical block. The accompanying toxemia quickly exhausts the patient, so that cough is ineffective. A vicious cycle is thus created, and tissue destruction continues unabated. The impaired circulation to the local area prevents antibiotics from reaching the infected site. The idea of emergency pulmonary resection is not without precedent. Sellors and his colleagues reported, in 1946, a series of patients with spreading pneumonitis, in whom emergency pulmonary resection resulted in a significant salvage not previously obtained with conservative measures. The incidence of complications in emergency pulmonary resection for acute necrotizing pneumonia, although somewhat higher than that observed with resection in advanced bronchiectasis, is of little significance when considered in relation to the marked reduction in mortality which appears possible. Further evaluation of emergency pulmonary resection in fulminating necrotizing pneumonias seems warranted.

Arteriovenous Fistula of the Kidney: New Observations and Report of Three Cases. C. H. Scheifley, G. W. Daugherty, L. F. Greene and J. T. Priestley. Circulation 19:662-671 (May) 1959 [New York].

The fact that all but 2 of the 12 previously reported cases of arteriovenous fistulas of the kidney have been reported in the past 11 years suggests that they are not as rare as is indicated by this small number. The authors present the histories of 3 patients with arteriovenous fistulas of the kidney, who were observed at the Mayo Clinic between 1954 and 1957. Two of them were women, aged 30 and 39 years, respectively, and one was a 42-year-old man. The term "arteriovenous aneurysm" has been widely used, but the fundamental lesion is a fistula, not an aneurysm. Data on all 15 patients are tabulated. The abnormal arteriovenous communications in the kidney and renal vessels in the 15 cases were thought to be congenital in 6, and to be due to trauma in 6 and to malignant tumors in 3. The causal trauma was a bullet wound in 3 patients, a stab wound in 1, and a surgical procedure in 1,

whereas the cause was uncertain in 1 of the 6 traumatic cases. Of the 6 arteriovenous fistulas listed as being of congenital origin, 2 were intrarenal, and 4 were in the renal vessels. There is evidence that in congenital arteriovenous fistula an eroding renal arterial aneurysm is etiological. In the 3 cases of malignant tumor of the kidney, including 1 of the 3 newly reported, erosion of the renal vessels by the tumor was the cause of the shunt.

The most notable features of arteriovenous fistulas are hypertension and cardiac enlargement with varying degrees of myocardial insufficiency. These features, particularly the hypertension, tend to set these fistulas apart from arteriovenous fistulas in other parts of the body. Peripheral arteriovenous communications do not result in hypertension and do not commonly result in heart failure. Hypertension is truly a hallmark of an arteriovenous fistula of the kidney.

Dramatic relief of heart failure and of lowered reserve followed corrective operation in every case in which these features were recorded; relief of hypertension followed corrective operation in 11 of 12 cases in which this feature was mentioned. A loud, diffuse, continuous bruit was invariably present. Preoperative and postoperative catheterization and indicator-dilution studies, angiograms, and aortograms were helpful diagnostic measures in the 3 cases presented. Arterialization of blood in the vena cava greatly increased cardiac output, and markedly shortened the recirculation time of the dye. Excretory urograms were abnormal in 11 of the 12 cases in which they were made. The mechanism producing hypertension appears related to loss of pressure, decrease in flow, and loss of pulsatile character in the renal artery distal to the fistula, giving a Goldblatt-kidney type of end-result. A vicious cycle of increasing hypertension followed by increasing flow through the shunt makes heart failure inevitable. The authors advise auscultation over the renal regions in patients with cardiac enlargement or failure of unknown causation, unexplained deformities in urograms, and renal tumors.

Carcinoma of the Gallbladder: Study of 17 Cases. D. Rosenberg, S. Carvalhal, J. A. de Mello Saraiva and H. Pucci. Rev. Assoc. med. brasil. 5:47-55 (Feb.) 1959 (in Portuguese) [São Paulo].

Carcinoma of the gallbladder is more frequent than is generally believed and is often associated with calculous cholecystitis. The authors report 17 cases of gallbladder cancer, in 13 of which biliary lithiasis was also present. In only 3 patients (17.6%) was a preoperative diagnosis of carcinoma of the gallbladder made. Differential diagnosis is difficult in a clinical picture that may simulate acute or chronic simple cholecystitis. Changes in the signs and symptoms, such as constant pain, loss of weight, intense jaundice, and palpable liver with nodules, are manifestations assignable to cancer. In 2 patients surgery was not feasible, and in 7 exploratory laparotomy only was performed. Cholecystectomy, however, was performed on 7 patients, and biliary–digestive tract anastomosis on 1. There were 10 immediate and 5 delayed deaths. One patient could not be followed up, but another has had an 8-year survival in excellent health; the latter patient had had a preoperative diagnosis of simple lithiasis, and only routine histopathological examination revealed malignancy. The most frequent type of cancer was solid adenocarcinoma, found in 13 patients (74.1%). Metastases involved the liver in 12 patients, the colon and stomach in 4, the peritoneum in 2, and the bones in 1. Because the diagnosis of gallbladder cancer is difficult and because the chronic irritating action of gallstones is an etiopathogenic factor in this type of primary carcinoma, cholecystectomy is indicated as soon as a diagnosis of calculous cholecystitis is made, even in cases of "silent" calculi.

Scalene Node, Parietal Pleura, and Lung Biopsy in the Diagnosis of Intrathoracic Disease. J. W. Smith, H. G. Parsons and A. C. Daniels. J. Thoracic Surg. 37:611-620 (May) 1959 [St. Louis].

An accurate diagnosis can often be made in pulmonary diseases by use of one or more techniques of biopsy which may spare the patient the morbidity, time, and expense associated with thoracotomy. These techniques, in addition to laboratory, roentgen-ray, and endoscopic procedures, include biopsy of the scalene lymph nodes, of the parietal pleura, and of the peripheral parts of the lung tissue itself. The authors discuss literature reports and their own experiences with these different techniques of biopsy at the Weimar (Calif.) Chest Center. They performed biopsy of the scalene node on 50 patients, in 2 of whom the procedure was done bilaterally. In 19 of these 50 patients, histological study of the scalene node material proved positive. This procedure is most useful in diagnosis of sarcoidosis, lymphoma, and metastatic malignancy. It is of particular use in determination of operability in carcinoma of the lung.

Biopsy of the pleura was performed on 25 patients. In only one of these had Mycobacterium tuberculosis been isolated from the pleural fluid; the biopsy was done after a year of therapy in this patient. In all remaining cases, acid-fast bacilli had not been found in pleural fluid, sputum, or gastric contents previous to biopsy. Many of these patients had no fluid present at the time they reached the hospital. The histological study of the biopsy specimen revealed tuberculous pleuritis in 17 of the 25 patients. One biopsy yielded a false-negative report, since the patient was later proved to have tuberculous pleural effusion. Pleural biopsy is of particu-

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lar value in the case of "idiopathic pleural effusion" or thickened pleura. It will often shorten the time required to make a diagnosis, even though such diagnosis could be made by other slower means.

Biopsy of the lung through a small incision was performed on 9 patients; in 3 of these tuberculosis was established, and various other lesions were found in the rest. The authors feel that lung biopsy is of value in cases of diffuse pulmonary infiltrations in which an accurate diagnosis cannot be made by other means. Sarcoidosis, pulmonary fibrosis, pneumoconiosis, and certain types of tuberculosis and metastatic malignancy, the diseases most commonly found by this method, are not amenable to surgical treatment, and there is no need for thoracotomy of the classic type for definitive treatment of the disease. The medical management varies in each of these conditions. Hence the importance of a correct diagnosis. Unfortunately, some of the specimens will not be diagnostic of a specific disease process. The clinician must always keep in mind the possibility of multiple disease processes. The diagnosis of tuberculosis, for example, does not exclude a carcinoma of the lung in the same patient. The addition of the 3 biopsy methods should reduce the number of "indefinite" diagnoses.

Staphylococcal Pseudomembranous Enterocolitis. J. T. McClellan and A. Balows. J. Kentucky M. A. **57**:551-553 (May) 1959 [Louisville].

The authors observed 21 patients with staphylococcic pseudomembranous enterocolitis during a period of 2½ years. The complication most frequently occurred in the treatment of diseases of the gastrointestinal tract, which included carcinoma of the esophagus, gastric and duodenal ulcer, obstruction of the small intestine, obstruction of the large intestine, ruptured appendicitis, carcinoma of the colon, diverticulitis of the colon, chronic ulcerative colitis, carcinoma of the gallbladder, chronic cholecystitis with stones, and carcinoma of the pancreas. The disease also occurred during the treatment of lymphosarcoma, tuberculous meningitis, congestive heart failure, pneumonia, kidney disease, and generalized vascular disease. In all these patients the disease developed after the use of either broad-spectrum antibiotics or combinations of antibiotics.

Effective treatment depends on early diagnosis. When staphylococci are found in the smears of the stool, cultures should be started, but treatment should not be delayed until the report of cultures and sensitivity. If the patient is receiving an antibiotic at the time the diagnosis is made, this antibiotic should be withdrawn, and the patient should receive instead one of the antibiotics known to be effective against the organism. It is essential that the antibiotic be given by the oral route in order to obtain the maximum concentration of the agent in the intestinal tract. The first choice among antibiotics is erythromycin, unless the patient was receiving this drug when the complication commenced. One of the newer antibiotics, such as ristocetin, novobiocin, or vancomycin, may be indicated if the organism is resistant to erythromycin. Fluids, electrolytes, blood plasma, and serum albumin are forced to combat the constant loss of fluid and to combat shock. While corticotropin has been reported by some authors to have dramatic effects against the toxicity of the enterocolitis, this has been denied by others, and it was not used in this series of patients. Seven of the 21 patients in this series died. Early diagnosis and vigorous treatment are essential.

Eosinophilic Granuloma of the Gastro-Intestinal Tract: Report of Two Cases. H. J. Toole and A. N. Moschopoulos. Brit. J. Surg. **46**:445-448 (March) 1959 [Bristol, England].

The authors report on 2 cases of eosinophilic granuloma of the gastrointestinal tract in a 14-year-old boy and a 55-year-old woman who were operated on at the Aretaion Hospital in Athens, Greece. The boy had recurrent attacks of colicky medial abdominal pain of 3 months' duration. The pain occurred in waves, lasting for a few minutes and gradually decreasing, and was associated with vomiting, constipation, and distention of the abdomen. The temperature was often as high as 102.2 F. (39 C). The attacks lasted for 2 or 3 days and usually disappeared after a bowel movement. The patient's general condition was good, although he had recently lost some weight. A plain roentgenologic examination after a barium meal revealed an obstruction in the ileum with a large dilatation above the obstructed area. On operation, a hard tumor, the size of egg, was found in the proximal part of the ileum. The tumor with an intestinal segment of 25 cm. was resected. The postoperative course was uneventful. Microscopic examination of the operative specimen showed inflammatory infiltrations consisting of polymorphonuclear leukocytes and plasmocytes. In many areas eosinophils were abundant, together with some cellular elements of connective tissue. No malignant cells were seen.

The woman had for 6 months a feeling of fulness and of burning sensation in the epigastric region, accompanied by nausea and a tendency to vomit; during the last 3 preoperative months these symptoms had increased, especially after eating. A barium meal examination revealed an oval, sharply defined filling defect in the bulb of the duodenum. On operation, a mass was found in the first part of the duodenum. It was pushed up by slight pressure and passed the pylorus easily. The stomach was opened along its anterior wall, to which a polypoid structure, 2 to 2.5 cm. in diameter, was attached by a short pedicle. A polypectomy was performed. The

postoperative course was uneventful. Microscopic examination of the operative specimen showed crowded accumulations of cells of moderate size and also some relatively small cells. The cells were elongated in form, or elliptical or spindle-shaped, and formed diversely arranged bundles. In some areas they formed whorls with numerous eosinophilic leukocytes. No malignant cells were found. Eosinophilic granuloma of the gastrointestinal tract is a clinical entity, characterized by the development of granuloma with eosinophilic infiltration. Most frequently this condition involves the pyloric region of the stomach; 34 such cases were collected from the literature. The condition is rare in the intestine, 7 instances in the small intestine and 5 in the large intestine being collected from the literature. The lesion appears in 2 forms, either as a real solitary tumor or as a diffuse infiltration, involving a small or a larger part of the digestive tube. The cause of the lesion is still unknown. Allergic factors or disturbance of the cell metabolism are suspected. In most of the cases collected from the literature, there was an increase in the white blood cell count and fever, which seemed to indicate an infection. The prognosis is good, as there was no recurrence in any of the cases. In pedunculated tumors polypectomy is the treatment of choice, while in sessile and diffuse forms resection of the affected area of the gastrointestinal tract should be performed.

Two Cases of Pulmonary Chorioepithelioma Submitted with Success to Surgical Therapy. J. Varangot, A. Granjon and S. Yannotti. Presse méd. 67:582-585 (March 25) 1959 (In French) [Paris].

Postpartum pulmonary chorioepitheliomas are considered serious, the patients usually dying of them within 6 months. Case reports have been published, though, which tell of the disappearance of roentgenographic evidence of pulmonary chorioepithelioma. This disappearance is claimed to be caused by physical therapy or by various medicinal or hormonal substances. A period of no therapy has also been followed by disappearance of the tumor. The authors report 2 cases of pulmonary chorioepithelioma cured by lobectomy and followed up for 4 and 6 years respectively. In the first case, the thoracic roentgenogram showed 2 opacities in the lung. There was much estrogen activity, and lobectomy disclosed a white encapsulated tumor. In the second case, at lobectomy a chorioepithelioma with discrete necrosis and hemorrhage appeared in places to be a homogenous tumor. Eleven days after the operation the level of chorionic gonadotropins was diminished.

These cases are of exceptional interest because there are few patients who undergo surgery for this condition. There is little necessity for hesitation before surgical intervention considering the present state of thoracic surgery. Thoracic surgery should come before hysterectomy, which may be obviated by the absence of evidence of a uterine tumor. It may be possible to observe the level of gonadotropic hormones after thoracotomy and perform a hysterectomy only upon observance of a rise in the curve of chorionic gonadotropins. However, conservation of the uterus, allowing future pregnancies, carries the risk that chorioepithelioma may occur later; yet in cases of single or even double metastases, it is sometimes possible to obtain long survivals.

Fatigue Fracture of the Pelvis and the Lower Extremity. C. C. Wang, C. W. Lowrey and R. L. Severance. New England J. Med. 260:958-962 (May 7) 1959 [Boston].

The authors report on 83 men, between the ages of 18 and 25 years, with a total of 97 fatigue fractures of the pelvis and the lower extremity, who were observed at the United States Army Hospital, Fort Chaffee, Ark., between December, 1955, and May, 1958. Of these 97 fractures, 4 were in the pelvis, 4 in the femur, 8 in the tibia, 6 in the os calcis, and 75 in the metatarsal bones. Fourteen patients had double fractures. These fatigue fractures occurred in recruits 4 or 5 weeks after the beginning of their basic military training, and were strikingly frequent in the midwinter season, when heavy clothing and boots were worn. Fatigue fracture was generally ushered in as an aching pain in the involved bone, the pain being constant and dull and promptly relieved by nonweight bearing. In fatigue fracture of the pelvis, the aching pain was often experienced in the perineal region, and was aggravated by forceful abduction and adduction of the thighs. Compression of the lateral and plantar aspect of the heel often produced pain in fatigue fracture of the os calcis. Of great diagnostic interest was the reproduction of pain at the fracture site by forceful percussion of the ends of the long bone or of the heel.

Radiographic findings were as follows. In 2 patients with fatigue fractures of the pelvis, the fracture lines were detected at the junction of the pubic and ischial bones. Callus formation was noted in the late stage of the disease. In the patients with fatigue fractures of the femur, the fracture lines occurred in the lower third of the shaft, about 15 cm. proximal to the knee. All fatigue fractures of the tibia occurred at the upper third of this bone, about 12 cm. distal to the knee. Seventy-one (95%) of the 75 fatigue fractures of the metatarsal bones occurred in the second and third metatarsals, at the middle and distal thirds of the shaft. It cannot be overemphasized that in some patients with early fatigue fracture radiographic findings may not have been sufficiently developed to be recognized. It is, therefore, extremely important to reexamine the involved parts 2 or 3 weeks after the initial procedure if a fatigue fracture is seriously considered.

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Conservative treatment, consisting of absolute rest in bed for 10 days, was usually sufficient for the relief of pain, and temporary immobilization of the extremities usually effected cure.

The differential diagnoses of fatigue fracture include pathological fracture or pseudofracture due to systemic disorders, benign and malignant bone tumors such as osteoid osteoma, osteogenic sarcoma, and Ewing's sarcoma, and infection such as osteomyelitis and periostitis. Difficulty in the differentiation of malignant bone tumor and fatigue fracture may often occur during the initial examination, but the clinical history of unaccustomed physical training in a recruit is of great assistance, and the rapid increase of periosteal reactions and the demonstration of a radiolucent fracture line or sclerotic zone across the shaft of the involved bone should render this benign condition readily recognizable.

GYNECOLOGY & OBSTETRICS

Observations on Spread of Mastitis Caused by Staphylococci in an Obstetric Clinic: A Contribution to the Problem of "Staphylococcus-Hospitalism." A. Ranft-Häussler and H. P. Pöhn. Deutsche med. Wchnschr. **64**:817-820 (April 24) 1959 (In German) [Stuttgart, Germany].

The authors report an increased occurrence of mastitis in an obstetric clinic in Frankfurt am Main, Germany, between January and March, 1957. Staphylococcus pyogenes var. aureus was isolated as the causative agent in 31 women with mastitis. The strains of Staphlococcus isolated from 28 of these women showed the phage aspect of lysogroup 1 (80/7/73), designated as M-type. In an attempt to explain the mode of spread of this causative agent, repeated examinations of specimens from the nose, pharynx, and nipples of the puerperae and their newborn infants were carried out, starting in March, 1957. Of 42 puerperae, only 2 of whom had mastitis, 40 (or their nursing infants or both), i. e., 95%, harbored staphylococci, and in 13 (31%) the causative agent was the M-type. In an additional 22 puerperae (52%), an additional strain of Staphylococcus of lyso-group 3 (7/77/42D), designated as N-type, was found, and various other types of staphylococci were observed in 24 puerperae. Of 25 members of the hospital staff, M-type staphylococci were found in 8 (32%), and N-type staphylococci were found in 2 (8%), but on repeated examinations the M-type was found in only 4 persons (16%). The M-type staphylococci were found in about 10% of the specimens of air and material. The M-type and N-type staphylococci were found in the puerperae only several days after their admission to hospital; this was in contrast to the various other types of staphylococci which were detected earlier.

The reported data justify the conclusion that these hospital infections are to be considered as disseminated infections which in most of the cases originate from patients with suppurative infections. These infections may be air-borne or may be transmitted by the nursing personnel as indirect carriers. A definite, virulent type of Staphylococcus organism, but not the ubiquitously present type of Staphylococcus, is responsible for the puerperal mastitis. To prevent the dissemination of virulent Staphylococcus types with a high tendency to spread, patients with suppurative diseases should be strictly isolated; they should be confined to separate rooms with special nurses and special instruments. Disinfection should be carried out currently and at the patient's discharge.

Synchronous Combined Abdominal-Vaginal Hysterocolpectomy for Cancer of the Cervix—A Report of Fifty Patients. J. Howkins. J. Obst. & Gynaec. Brit. Emp. **66**:212-219 (April) 1959 [London].

The author reports on 50 women with carcinoma of the cervix, who underwent synchronous combined abdominovaginal hysterocolpectomy. The only operative death was unnecessary and avoidable since faulty management of a drip transfusion resulted in a fatal air embolism 7 hours after the operation; autopsy revealed that the operation could in no way be blamed for this fatality. This operation does not need to carry a greater mortality than the ordinary Wertheim operation. In 21 patients, urinary complications occurred, such as rectovaginal fistula, mild or transient stress incontinence, complete incontinence due to incompetence of the urethra, and loss of bladder sensation but no incontinence. There can be little argument that the synchronous combined abdominovaginal hysterocolpectomy is the most extensive operation yet devised for the removal of a cervical cancer and its potential lymphatic extensions. The criterion of a successful operation is a clean and empty pelvis, bounded above by the external iliac vessels cleared of all lymph nodes and cellular tissue, laterally by the naked obturator internus and levator ani muscles, and below by the vaginal introitus. Anteriorly the bladder, posteriorly the rectum, and laterally the ureters and obturator nerves are the sole remaining tenants. At the completion of such a dissection, the surgeon may feel confident that local recurrence is unlikely, and, in those patients in this series in whom subsequent surgical intervention or autopsy has been performed, the true pelvis has been found to be remarkably clear of growth, and any metastases present to be strictly extrapelvic.

Two instruments are strongly recommended for the control of pelvic hemorrhage. The first is Blalock's bulldog clamp, applied to one or both common iliac arteries, which effectively controls arterial

bleeding from the branches of the hypogastric artery. The second instrument is Paterson's long-shank clip forceps which provides the best method of controlling venous hemorrhage from the tributaries of the hypogastric vein. The extensive removal of the parametrium and paracolpium, which is ideal from the point of view of treating cancer, is achieved at the risk of denervating the bladder. This has resulted in considerable bladder malfunction, stress incontinence, residual urine, and loss of bladder sensation. This serious complication, which is the great drawback of the extensive operation, is the main point on which it may be justifiably criticized. It is difficult to know how much the surgeon is right to prejudice the integrity of an adjacent structure when attacking the cancer, though he should be prepared to accept the risk of injury to such structures if he is thereby more certain of thoroughly eradicating the malignancy. When, therefore, the tumor has extended down the vagina for a considerable distance, it is logical and proper to remove all this structure and all the paracolpium into which malignancy may have spread. The ultimate greater safety of the patient considerably offsets the disadvantage of the urinary complications.

Evaluation of Ovarian Functional Phases on the Endometrium with the Aid of Histochemical Reactions: Acid and Alkaline Phosphatase, Phosphoamidase and Glycogen Stains. J. Berger and E. Mumprecht. Schweiz. med. Wchnschr. **89:**433-439 (April 18) 1959 (In German) [Basel, Switzerland].

Cyclical changes in the activity of enzymes of the endometrium indicate a close relationship between these enzymes and the sex hormones. The authors were interested especially in the presence of the enzymes and in the changes which occur in the course of the ovarian cycle in the activity of acid phosphatase, alkaline phosphatase, and phosphoamidase and, in comparison with these, in glycogen and the polysaccharides. Curettage material from 40 women was fixed in acetone, embedded in paraffin, and sectioned. It was found that: 1. The acid and alkaline phosphatase content of the glandular epithelium increases with increasing estrogen effect in the course of the cycle. 2. Acid phosphatase can be found in the cytoplasm as well as in the nuclei of the glandular cells; it appears at the onset of the proliferation phase and reaches a maximum shortly before the rupture of the follicle. 3. Alkaline phosphatase, on the other hand, appears only late during the phase of proliferation; it also reaches a maximum just prior to ovulation, and it decreases abruptly during the secretory phase. 4. Phosphoamidase which characterizes the nuclear structure shows no marked changes during the menstrual cycle. It could be demonstrated that, like the hormonal cytodiagnosis of Papanicolaou, the acid and alkaline phosphatase activities are sensitive indicators of the effects of the sex hormones. The authors illustrate the dependence of enzyme reactions on hormonal influences in 2 women with varying degrees of estrogenic activity.

The Excretion of Chorionic Gonadotrophin by Women with Chorioadenoma and Choriocarcinoma. B. M. Hobson. J. Obst. & Gynaec. Brit. Emp. **66:** 282-287 (April) 1959 [London].

The author reports on 11 women, between the ages of 22 and 46 years, with chorioadenoma and on 18 female patients, between the ages of 11 and 49 years, with choriocarcinoma, all of whom underwent hysterectomy and from most of whom specimens of urine were obtained before and after the operation for quantitative estimation of the amounts of chorionic gonadotropin excreted in the urine. Before hysterectomy the amounts of gonadotropin excreted in the urine by both groups of patients were similar. Postoperatively the patients with choriocarcinoma continued to excrete large quantities of gonadotropin, which was presumably produced by metastases, up to the time of death. Of the 18 patients with choriocarcinoma, 3 are still alive, and in them the Xenopus (Hogben) test finally became negative. The urine from the women with chorioadenoma contained no measurable amount of gonadotropin 4 weeks after the hysterectomy. Because of this difference, the estimation of gonadotropin excreted in the urine after hysterectomy is a valuable aid to diagnosis. It also provides a measure of the effectiveness of any treatment. After the removal of the primary choriocarcinoma, 6 of the 18 women received roentgen irradiation for metastases. Five of these women died, and in only one was the reduction of metastases and the suppression of gonadotropin excretion in the urine followed by recovery. The chances that a patient with choriocarcinoma will recover are apparently extremely small. The 11 women who had a chorioadenoma and no postoperative therapy are all living 2 to 8 years after hysterectomy.

A New Problem of Fetal Cardiology: Atrial Fibrillation "in Utero." J. Reygaerts. Gynéc. et Obst. **58:**208-219 (April-May) 1959 (In French) [Paris].

Fetal electrocardiograms made during pregnancy, used by the author for the last year and a half as a guide in the study of fetal circulatory physiology, have proved especially valuable in the diagnosis of intrauterine life and death. A wave with a frequency of from 120 to 180 a minute provides assurance that the fetus is alive. The absence of such a wave suggests fetal death, but in about 3% of cases an abundance of amniotic fluid or of vernix caseosa leads to a false-negative result.

An abnormal wave with a very rapid irregular rhythm (360 to 420 a minute), presenting the characteristics of atrial fibrillation, was recorded in 4

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tracings. Two of the infants concerned died in utero, and the other two died a few hours after birth. Two of the deaths were related to severe Rh-isoimmunization. Two hypotheses may be envisaged: either the atrial fibrillation is a sign of imminent fetal death or it is a primary disorder and a cause of death. An analysis of the arguments in favor of each of these hypotheses, taking into consideration the findings in these 4 cases and pertinent data obtained from the literature, seems to support the belief that the disorder is primary. A possible cause of the atrial fibrillation may be cardiac decompensation with dilatation of the right atrium. Acute and chronic anoxia, too, may be suspected.

The birth of two of the infants alive suggests that the prognosis is not necessarily fatal and that it may be modified by appropriate therapy. The following measures are proposed: induction of labor, which should proceed as rapidly as possible (cesarean section is not advised, because the chances of fetal survival seem too slight); administration, to the mother, of digitalis glucosides and genuine antifibrillant medications; oxygen therapy; and bleeding of the newborn infant through the umbilical vein. The removal of, say, one-tenth of the infant's blood volume, or about 30 cc., may be expected to have a beneficial effect, probably because it suppresses the dilatation of the right side of the heart and diminishes its work.

It is to be hoped that fetal electrocardiography, having revealed the existence of this severe circulatory disorder, will make it possible to save some of these sick children by the institution of effective therapeutic measures. It will thus help to reduce perinatal mortality in its least understood and most distressing form—death at the end of pregnancy.

PEDIATRICS

Marking-Ink Poisoning: An Outbreak of Methaemoglobin Cyanosis in Newborn Babies. D. H. E. Ramsay and C. C. Harvey. Lancet 1:910-912 (May 2) 1959 [London].

The authors report an outbreak of aniline-dye poisoning by unfixed marking-ink in 6 newborn infants in the nursery of a maternity home of 22 beds. The 6 patients were affected simultaneously with cyanosis. This was mild and symptomless in 5 and disappeared within 24 hours. One infant, who was the first to show cyanosis and who was placed in an oxygen tent for this reason, was severely affected and had cerebral irritation and prolonged twitching while being treated. The patient was given methylene blue intravenously with dramatic and complete recovery of normal color. None of the 5 other infants required any specific treatment, apart from removal of the source of intoxication when it was discovered.

At this maternity home all napkins have for some years been marked by a sewing machine, and the use of marking-ink had long been discontinued. Due to domestic circumstances, as new members of the staff were unaware of the reason for long-standing safeguards, 72 new napkins were issued from the stock and were immediately marked with the maternity-home name stamp, a bottle of old marking-ink, which had been on the shelves for more than 8 years, being used. The napkins were made available for use without being laundered first. The first infant became cyanosed 3 hours later. In the oxygen tent he was subjected to the added hazard of intense rebreathing of aniline vapor, whereas the other 5 infants were exposed only to the chance of skin absorption and inhaling vapor as they lay in their cots.

Direct skin absorption and inhalation of vapor can convert the hemoglobin of the red blood corpuscles into methemoglobin to an extent which endangers life. Methylene blue given intravenously acts by virtue of its reversible catalysis of tissue reduction and oxidation, the change from methemoglobin to hemoglobin being one of reduction. Renewed publicity needs to be given every year to the importance of fixing marking-ink before garments are used, and this subject might be given prominence in all refresher courses for midwives.

Ulceronecrotic Enterocolitis of the Premature. A. Rossier, S. Sarrut and J. Delplanque. Semaine hôp. Paris 35:1428-1436 (April 24) 1959 (In French) [Paris].

Ulceronecrotic enterocolitis occurs in small epidemics in centers for premature infants, rather than in widespread epidemics such as those caused by pathogenic colibacilli. The cases usually appear sporadically, stretched out over the course of a year, without seasonal predominance. The disease affects premature infants almost exclusively; the few infants born at term in whom it has been reported have almost all had a birth weight of less than 2,500 Gm. (5½ lb.). The 15 infants personally observed by the authors weighed from 900 to 1,690 Gm. (2 to 2½ lb.) at birth.

The initial period of the disease usually begins between the 10th and 30th days of life and lasts from 4 to 10 days, during which vague signs suggesting merely ordinary dyspepsia appear. A deceptive calm follows in about one-third of the cases; the child's weight begins to increase again, its general condition improves, and the digestive disturbances diminish—all of which leads to the erroneous belief that a transient state of dyspepsia has been overcome. The calm lasts for 1 or 2 weeks, sometimes even longer, and then the digestive disturbances reappear; diarrhea occurs and is followed more or less abruptly by a complete cessation of bowel movements, sometimes suggesting acute oc-

clusion. Vomiting is constant; abdominal distention increases; and the general condition deteriorates. This development in 3 phases, though characteristic, is not invariable; quite often, the disease appears suddenly in a child who had previously seemed to be doing well.

The principal anatomic lesion consists of one or more intestinal perforations at points of necrotic ulceration in the intestinal mucosa, usually in the ileocecal region. Secondary septic peritonitis follows, and recovery is exceptional. One of the authors' 15 patients was successfully operated on, but they know of no other instance of cure in a premature infant. The diagnosis was established early in the case referred to, and the operation, an ileocolectomy performed by a team skilled in surgery on newborn infants, was carried out while the child was still in good condition.

Local ischemia, revealed by histological study of autopsy specimens, seems to be the underlying phenomenon, leading either to direct perforation or to ulceration followed by perforation. Inflammatory phenomena, when present, are due to the secondary peritonitis. The cause of the disease is obscure: the bacteriological findings are not significant, but the possibility of a viral infection cannot be excluded. Infection, whether bacterial or viral, however, does not adequately explain all the characteristics of the lesions, and an important role in their causation must be ascribed to the vasomotor reactions proper to the premature terrain.

Pyridoxine-Sensitive Convulsive Attacks in the Newborn and the Nursling. J. Marie, A. Hennequet, G. Lyon and others. Semaine hôp. Paris **35**:1411-1421 (April 24) 1959 (In French) [Paris].

A rare syndrome characterized by neonatal convulsions responding only to pyridoxine (vitamin B_6), first described by Hunt and co-workers in 1954, was observed in a 15-day-old infant admitted to the authors' service with a diagnosis of cerebromeningeal hemorrhage. The child's parents were healthy, and he had one sibling, a clinically normal 17-month-old girl. He was born at term after a normal pregnancy of 8½ months. Labor lasted for 4 hours, and the infant was delivered naturally without the use of either anesthesia or forceps. His birth weight was 2,900 Gm. (6½ lb.), and he cried at once. He was breast-fed, with supplementary feedings of half-skim milk. Fairly intense physiological jaundice appeared on the 2nd day and lasted until the 10th day. Generalized convulsive attacks, which began on the 5th day of life and occurred intermittently during the first month, became virtually continuous during the second month, producing a convulsive state refractory to standard anticonvulsive therapy. Hypocalcemia and hypoglycemia were excluded as possible causes. Vitamin B_6 was then suggested; all anticonvulsive medication was discontinued, so that the effect of the vitamin could be accurately evaluated; and the child was given 250 mg. of pyridoxine by mouth, in 2 equal divided doses, in 24 hours. The result was surprising: in less than 24 hours the convulsions had stopped; the baby was tranquil and somnolent, although he woke up normally in time for his feedings and took them without difficulty.

The remarkably beneficial effect of vitamin B_6 was then verified by a series of therapeutic tests in which it was given in various doses, intramuscularly, intravenously, and orally. The intravenous injection of 10 mg. was followed in only a few minutes by the disappearance of convulsive movements and the return of the electroencephalographic tracing to normal within 24 hours. Interruption of vitamin B_6 therapy was followed by the reappearance of convulsions after a period of about 5 days. The symptom-free period seems to be invariable for an individual patient, but variable from one patient to another; thus, in Hunt's original case, it was 48 hours. Continuous vitamin therapy was accompanied by the complete cessation of convulsive attacks and consistently normal electroencephalographic tracings. A maintenance dose of 4 mg. by mouth was needed to secure this result; administration of amounts below this threshold dose led first to the reappearance of electroencephalographic anomalies and then to convulsions.

Nothing was found on clinical or encephalographic examination to explain the occurrence of this syndrome, which seems to be unquestionably due to a congenital disturbance in metabolism. The fact that psychomotor retardation was present in the authors' patient and in 2 of the other 3 infants in whom this syndrome has been reported, whereas one child is apparently normal, suggests that treatment with vitamin B_6 should be started without delay whenever a convulsive state of unknown origin resistant to the usual forms of therapy develops in a newborn infant or a nursling. It should be noted that the amount of vitamin B_6 required by these children is from 10 to 30 times greater than that physiologically required by normal infants of their age.

Steroid Therapy in Some Types of Post-infectious Encephalomyelitis. G. Öberg. Acta paediat. (supp. 117) **48**:56-60 (April) 1959 (In English) [Uppsala, Sweden].

The author reports on 6 children, between the ages of 7 and 15 years, in whom neurological complications, such as Guillain-Barré syndrome (virus encephalomyelitis), coma, convulsions, and headache associated with fever, occurred after measles, chickenpox, and rubella, respectively. The very severe course in one of these children made it necessary to perform tracheotomy and to employ a positive-pressure respirator; the child recovered,

although there was some residual disturbance. Of the other 5 children, 3 were treated with cortisone and 2 with prednisone. Cortisone was given in daily doses of 100 to 50 mg. for 3 to 5 days. Convalescence lasted from 2 to 4 weeks, and there were no sequelae. Prednisone was given in daily doses of 30 to 15 mg. for 3 or 4 days. There was slight improvement during the first days of treatment with this steroid. Despite continued therapy the patients became worse again; one of the 2 became worse when the dose of prednisone was reduced, and the electroencephalogram was still abnormal 10 months after therapy.

The neurological complications of the contagious exanthems may be very severe and dangerous. Residual symptoms are not uncommon. Even transitory anoxemia can cause cerebral lesions. Treatment by tracheotomy and respirator is sometimes lifesaving. There is much evidence in support of the opinion that neurological signs after measles, chickenpox, and rubella are of anaphylactic origin. Attempts at steroid therapy may be justified. Treatment should be applied only for a few days, and then only during a stage of the illness when good antibody production can be counted on. Until more may be known about the efficacy of this therapy, it should be reserved for severe cases with signs of cerebral edema or cranial nerve paralysis.

Primary Acute Cardiac Insufficiency in Infants Under the Age of Two. S. Cavalieri and P. Montenovesi Minerva pediat. 11:258-272 (March 10) 1959 (In Italian) [Turin, Italy].

The authors believe that primary acute cardiac insufficiency in the first period of life is a more frequent disease than is usually recognized. An acute respiratory or gastroenteric disorder may mask the underlying lesion. The series reported included 25 hospitalized infants, aged up to 24 months, 15 of whom were males. Myocarditis was present in 10 patients, a nonidentifiable heart disease in 5, fibroelastic myoendocarditis in 4, high irregularity in the heart sounds in 2, and myocardiosclerosis in 1. The earliest and most frequent prodromal symptom (18 instances) was a state of high agitation, during which the infant had a painful look, wept, refused food, and could not sleep. Subsequently dyspnea developed in 23 infants; it was accompanied less frequently by cough (9 instances), gastrointestinal disorders (2 instances), and sweating (8 instances).

The specific symptoms of primary acute cardiac insufficiency were an agitated state, frequent sweating, and pale and grayish skin. The dyspnea which developed in 23 patients (95%) was accompanied by cyanosis in 10 instances (40%). Cough appeared more frequently than in the prodromal phase. Tachycardia was present in all the patients, and psychomotor disturbances in 17 (70%). Enlargement of the heart (not necessarily considerable or roundish) took place in all the patients but was demonstrated on percussion in only 14 instances (56%). Enlargement of the liver and changes in the electrocardiographic pattern followed. Among the less frequent specific symptoms were vomiting, diarrhea, and fever. The laboratory findings were not illuminating. Eleven patients (77%) died within a few hours, and 4 died within 2 years after onset of the disease.

Pneumoencephalography in Early Infancy—Risks, Clinical Indications and Technical Considerations. B. Hagberg, A. Hamfelt, M. H. Holmdahl and H. Lodin. Acta paediat. (supp. 117) 48:61-68 (April) 1959 (In English) [Uppsala, Sweden].

The authors obtained 123 encephalograms from 122 infants and children at the University Hospital in Uppsala, Sweden, between 1951 and 1956. Thirty-five of the 122 patients were aged less than 2 years. Of these 35 patients, the main clinical diagnosis in relation to the type of brain damage was cerebral palsy in 10, mental retardation in 12, epilepsy in 2, hydrocephalus in 8, and acute neurological disorders in 3, including glioma of the pons, and subdural effusions due to encephalitis and suppurative meningitis, respectively. Of 31 successfully performed encephalograms, 29 gave abnormal results. Strikingly similar encephalographic changes with more or less central and cortical atrophies were found in patients with mental retardation, cerebral palsy, and epilepsy without other neurological symptoms. Thus, the roentgenologic findings were by no means pathognomonic of any of these disorders. There was no good correlation between the degree of atrophy and the severity of the clinical picture.

Slight untoward reactions to the pneumoencephalogram, consisting of mild or moderate fever for a few days, nausea, headache, and/or slight meningeal irritation, were present in 59 of the 122 patients, but seemed to occur less frequently in young infants than in the older age group. Serious reactions occurred in 6 patients, 4 of whom were less than 1 year old and the 2 others were, respectively, 14 months and 4 years of age. Three of these reactions occurred during the encephalographic examination, and 3 within hours after the examination. In only 1 of the 6 patients, in whom difficulties in endotracheal intubation were observed, could the complication be considered technically avoidable. In the other 5 patients, the suddenly developing cardiovascular or breathing disturbances most likely were of a central origin, possibly unavoidable in a complete fractional encephalography. In all 6 children general anesthesia was used. In the older, quiet children the examination was carried out with the aid of slight sedation. From the experiences gained in this series it appears that the only strong

indications for encephalography in early infancy are patients with progressive hydrocephalus or those in whom an expanding nonsubdural intracranial lesion is suspected. It seems desirable to keep strictly to these indications in the younger age group. In older children, encephalography can be performed on more relative indications and may sometimes be valuable in the investigation of nonprogressive neurological disorders.

On the Use of Exchange Transfusion in Neonatal Thrombocytopenic Purpura: Report of a Case. A. Killander. Acta paediat. (supp. 117) 48:29-33 (April) 1959 (In English) [Uppsala, Sweden].

The author reports on a male infant with neonatal thrombocytopenic purpura, whose birth weight was 8½ lb. (3.9 kg.) and in whom several small petechiae scattered over the whole body were observed 11 hours after birth. A few ecchymoses were found on both arms. Further studies revealed a platelet count of less than 10,000 per cubic millimeter. There were no neurological symptoms and no signs of intestinal bleeding. The spleen was not palpable. Both mother and infant had blood group A, type Rh+. A blood count of the mother revealed nothing abnormal except for an abnormally low number of platelets, namely, 74,000 per cubic millimeter. The following day the infant's platelets were still less than 10,000 per cubic millimeter, and an exchange transfusion was performed; 530 cc. of fresh blood was injected by way of the umbilical vein, and the same amount was removed. The day after the exchange transfusion the number of platelets had increased to 40,000 per cubic millimeter, but afterwards it began to decrease. No new bleedings were noted, and the infant was discharged from hospital on the 15th day after birth. Two weeks later the mother noticed some red, bloodlike streaks in the infant's stool, and he was readmitted to hospital. On admission a few small petechiae were noted on the palate and on the body. The bone marrow obtained by tibial puncture showed a reduced number of megakaryocytes with degenerative signs. During an observation period of 9 days, no intestinal or cutaneous bleedings were observed, and the infant was discharged again. During the second stay in the hospital the platelet count remained less than 15,000 per cubic millimeter, but when the patient was seen at the outpatient department at the age of 49 days, the platelet count had increased to 60,000 per cubic millimeter. Since then the recovery has been uneventful.

The mother had not had abnormal bleeding before or during delivery, and the disease would have remained undiagnosed if the infant had not shown a petechial rash after birth. The number of platelets in the mother was constantly below normal for 4 months after delivery, and it seems most likely that she had a mild form of idiopathic thrombocytopenia. The disease in the infant was possibly due to platelet antibodies transferred from the mother. Thrombocytopenia and bleedings, which are sometimes found in severe cases of hemolytic disease of the fetus and newborn infant, usually subside after exchange transfusion. By treating congenital thrombocytopenic purpura with exchange transfusion, a similar result might be attained. Because of the high mortality during the first days after birth, neonatal thrombocytopenic purpura demands special attention, so that treatment can be instituted immediately after birth if necessary. Splenectomy seems to be contraindicated in view of the fact that the disease is self-limited. Compared with other methods of treatment, exchange transfusion seems to be the best. Women with idiopathic thrombocytopenic purpura should be delivered in hospitals with exchange transfusion units and laboratories for hematological serology.

DERMATOLOGY

Lichen Myxedematosus (Papular Mucinosis Dalton and Sidell): Report of an Additional Case. S. J. Zakon, J. H. Johnson and H. Grinvalsky. A. M. A. Arch. Derm. 79:519-523 (May) 1959 [Chicago].

The authors report a case of lichen myxedematosus observed in a 55-year-old woman in the fall of 1956. Lichen myxedematosus must be distinguished from scleroderma, neurodermatitis, lichen ruber moniliformis, myxedema, amyloidosis, lichenoid tuberculids, and other lichenoid eruptions. While the histopathology in all the mucoid diseases is characterized by excess accumulation of mucin, the differentiation from myxedema and from pretibial myxedema is made on the basis of absence of thyroid and other endocrine disease. Despite the fact that there has been considerable research on the metabolism of mucopolysaccharides, there have been no definite conclusions as to the etiology and pathogenesis of lichen myxedematosus. The disappearance of the positive reaction after hyaluronidase digestion, observed in this case, lends some support to the proposition that the edema in lichen myxedematosus is related to an increase in hyaluronic acid. Concerning the theoretical explanation that either lichen myxedematosus is due to an imbalance of hyaluronidase and hyaluronic acid or a blocking agent to hyaluronidase exists, it may be stated that hyaluronidase has not been conclusively demonstrated to occur in mammals in locations other than the testicular tissues. It is presumed that other enzyme systems are concerned with the synthesis and breakdown of mucopolysaccharides, but their exact nature is as yet unknown. Clinical diagnosis without histopathological studies is prac-

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tically impossible. The use of the acid mucopolysaccharide stain not only proved to be effective but also allowed unmistakable interpretation.

The Pathogenesis of Superficial Fungous Infections in Cultured Human Skin. H. Blank, S. Sagami, C. Boyd and F. J. Roth Jr. A. M. A. Arch. Dermat. 79:524-534 (May) 1959 [Chicago].

This study on fungous infections provides data to suggest that there are humoral factors which ordinarily bar invasion by dermatophytes but that in appropriate circumstances the organisms will readily invade living nonkeratinous skin. More than 500 pieces of skin, grown on a wide range of mediums and by many techniques, inoculated with fungal pellets, were used for the authors' experiments. These experiments demonstrated that dermatophytes are prevented from invading the living epidermis and dermis by the fungistatic effect of normal serum. Decreasing concentrations of the serum permit deeper invasion. The substances which produce fungistasis are not yet known. Neither gamma globulin nor other protein fractions, such as albumin and fractions II, III, or IV, seem to possess such activity. Dialysis and heating (56 C) diminish the antifungal activity of serum when tested in infected organ cultures. Both procedures used in the experiments reduced the fungistatic effect, but neither destroyed it completely. The authors suggest that further study of the host factors would be a rewarding direction of mycologic research. By manipulating the tissue milieu in which the fungi grow, it may become possible to understand and affect the factors which result in clinical resistance and susceptibility to disease.

Neurilemmoma of the Tongue. E. S. Mercantini and C. Mopper. A. M. A. Arch. Dermat. 79:542-544 (May) 1959 [Chicago].

The authors present a review of the clinical picture, histopathology, pathogenesis, and treatment of neurilemmoma (schwannoma); it is demonstrated by a report on a 22-year-old man, seen in May, 1958, in whom such a lesion occurred on the tongue. The lesion was shallow, 2 mm. in diameter, slightly edematous, and tender and suggested an aphthous ulcer or herpes simplex infection. The lesion healed quickly, but soon thereafter at the site of the previous ulceration a nodule made its appearance and grew to the size of a split pea within a period of 12 days. This second lesion was excised completely, the gross specimen being mushroom-shaped, with a fairly broad but short stalk, about 2 mm. long. The undersurface of the lesion revealed a number of small millet-sized and millet-shaped grains which were attached loosely by small strands. The lesion was composed of spindle cells frequently arranged in palisaded fashion; between the nuclear palisades there was a small amount of finely fibrillar tissue, which stained as connective tissue with van Gieson's stain. As regards the pathogenesis, such a lesion is a neoplasm which arises from the sheath of Schwann spontaneously or possibly secondary to trauma or irritation of the involved nerve trunk; in this case, the onset of the lesion was preceded by trauma.

Neurilemmomas usually are solitary and affect women more frequently than men, without particular affinity for any age group. They occur commonly on the cranial nerves and as peripheral lesions, which are found on nerves in the scalp, face, sides of the neck, tongue, flexures of the arms, wrists, knees, and ankles, and walls of the stomach, intestines, and aorta. In a minority of cases the tumors are multiple or are accompanied by neurofibromatosis. Hence, the finding of a single neurilemmoma should lead to a careful examination of nerves elsewhere on the body, even though this may prove fruitless in most cases.

Dermal Changes Following Abrasion. S. Ayres, J. W. Wilson and R. Luikart. A. M. A. Arch. Dermat. 79:553-568 (May) 1959 [Chicago].

The authors report clinical and histological observations made on 13 patients in whom abrasion of the skin was carried out for therapeutic or experimental purposes. The majority of the patients were between the ages of 70 and 80 years and presented multiple recurrent actinic keratoses of the face; some relatively young people had acne scars of the face. The abrasions were performed with a motor-driven rotating abrasive instrument. Forty-three biopsy specimens were obtained, and from these about 500 microscopic slides containing some 3,600 stained sections were examined.

Experiments revealed that, after abrasion to a moderate depth, the dermis begins to regenerate once the epidermis has finished regenerating. This occurs at about one week on the face and at 10 days on the back. After abrasion to a moderate depth of 1 mm., comparable to that attained in abrading acne pits of average depth, dermal tissue regenerates substantially, but not completely, so that the thickness of the skin after abrasion is 85 to 90% of its original thickness. The newly regenerated dermal tissue at first stains as reticulum, but by 2 months after abrasion it stains as mature collagen and has a horizontally striated pattern. The skin after abrasion is relatively hypopigmented in fair-complexioned persons, in contrast to the adjacent actinically damaged areas. The failure of the previously abraded areas to approximate the color of the adjacent actinically damaged senile skin is undesirable from a cosmetic standpoint and indicates the necessity of abrading large areas evenly and without leaving intervening gaps. When the prevention of skin cancer is the chief objective, then this consideration is less important.

The abraded skin areas are considerably less prone to develop actinic keratoses than the adjacent nonabraded areas. Therefore, abrasion is relatively effective in the prophylaxis of premalignant lesions, although not as completely as would be anticipated on theoretical grounds alone. After abrasion, basophilically degenerated collagen in the upper cutis is replaced by normally staining collagen. A corresponding clinical change occurs, so that the regenerated skin is more elastic and youthful appearing than is that of the adjacent actinically damaged areas.

THERAPEUTICS

Vancomycin: Report on Treatment of Patients with Severe Staphylococcal Infections. A. A. Dutton and P. C. Elmes. Brit. M. J. 1:1144-1149 (May 2) 1959 [London].

The authors report on 9 patients with severe staphylococcic infections, who were treated for a 9-month period, beginning in November, 1957, at Hammersmith Hospital, London, with vancomycin. Only 3 of these 9 patients demonstrated normal renal function. The infecting strains of Staphylococcus organisms were all resistant to several antibiotics, and treatment with other antibiotics had failed. Vancomycin therapy led to a good clinical response. Two of the 9 patients died when vancomycin was withdrawn before the infection was controlled. Two other patients recovered from the staphylococcic infection but died subsequently of septicemia due to Pseudomonas aeruginosa. Vancomycin was effective in the remaining 5 patients.

Although vancomycin is bactericidal in vitro, 3 of the 5 surviving patients continued to harbor the infecting staphylococci in lesions. The danger of drug deafness in uremic patients is stressed. This may occur during or after treatment. Several uremic patients developed toxic deafness on dosage of 1 or 2 Gm. daily, although none received more than 13 Gm. in the course of treatment. A regimen of lower doses controlled by "rapid" serum assays is outlined. This regimen was used successfully in the management of a uremic patient with staphylococcic pneumonia, a total of 5.125 Gm. of vancomycin having been given over 11 days. Thrombophlebitis occurred in some patients when the vancomycin was given by simple intravenous injection in 10 ml. of saline solution, but this condition did not occur when it was administered in 250-ml. infusions over a 30-minute period or in larger volumes in saline or 5% dextrose transfusions. Since the drug is toxic to the 8th nerve, it is likely to be used mainly in hospitals for severe staphylococcic infections, especially in those cases in which the staphylococci are resistant to several other antibiotics or in which chemotherapy is otherwise unavailing. It is also valuable when a bactericidal drug is particularly desirable in patients whose normal defense mechanisms are defective.

Trypsin in Peripheral Vascular Diseases: Review and Report on Treatment of 210 Patients. H. Murphy. New York J. Med. 59:1973-1980 (May 15) 1959 [New York].

Crystalline trypsin, a proteolytic enzyme, was shown to have an ameliorating effect on the acute signs of thrombophlebitis, including reduction of pain, swelling, and redness. The author reports on a survey of 210 patients with peripheral vascular diseases, who received ambulatory treatment with crystalline trypsin (Parenzyme Aqueous) for 4 to 16 months. The patients ranged in age from 26 to 80 years. Most of them, particularly those with lymphedema and varicose veins, had been treated extensively elsewhere by many different methods with unsatisfactory results. The patients were given intramuscular injections of 2.5 mg. of crystalline trypsin once daily during the acute stage of the disease. When acute inflammation subsided, the dose was reduced to 2.5 mg. 3 times a week.

Of the 210 patients, 160 showed excellent results, 44 good results, and 6 poor results. Particularly encouraging results were obtained in patients with chronic varicose ulcers, superficial venous thrombosis, acute phlebitis with ulcers, dermatitis and/or cellulitis, and acute superficial thrombophlebitis. Fair results were obtained in cases of chronic deep thrombophlebitis with lymphedema, but this group still presents a challenge; probably irreversible tissue changes inhibit the accessibility of the thrombolytic and antiphlogistic actions of trypsin. Two patients presented generalized urticarial reactions, and there were local reactions in about 14% of the 210 patients, necessitating discontinuation of trypsin injections.

Kanamycin—A New Antibiotic: Treatment of 22 Patients with Infection of Urinary Tract. K. Nørredam and L. M. Pedersen. Ugesk. laeger 121:611-617 (April 16) 1959 (In Danish) [Copenhagen].

Treatment with kanamycin was applied in 22 patients with infections of the urinary tract, 21 of them with chronic pyelonephritis. In most cases the urine became free of bacteria and leukocytes during the treatment, but it was often reinfected, sooner or later, after the treatment ended. In 4 patients mild to marked reduction of hearing developed. The danger of impairment of hearing seemed to be greater in patients with poor renal function. The authors advise that until the toxicity of this new broad-spectrum antibiotic is better known, kanamycin should be reserved for infections of the urinary tract which are resistant to other less toxic antibiotics or chemotherapeutics.

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Autologous Bone Marrow Infusion as an Adjunct in Therapy of Malignant Disease. W. McFarland, N. B. Granville and W. Dameshek. Blood 14:503-521 (May) 1959 [New York].

Attempts to eradicate malignant lesions by methods such as irradiation or chemotherapy are frequently limited by the vulnerability of normal tissues, particularly bone marrow, gastrointestinal tract, and skin. Efforts to restore the marrow after massive roentgen irradiation or after chemotherapy by means of homologous bone marrow transplantation have been unsuccessful, probably because of the development of an immune reaction between host and transplant. The use of the patient's own (autologous) bone marrow circumvents this reaction and theoretically should permit higher dosage in roentgen irradiation or chemotherapy with subsequent bone marrow recovery. The authors tried this method in "terminal" cases. Three patients with lymphosarcomatosis and 2 with disseminated Hodgkin's disease were treated with massive doses (superdosage) of nitrogen mustard (over 1 mg. per kilogram of body weight) given intravenously, followed by the intravenous infusion of autologous bone marrow. Two of the 5 patients succumbed to infection. The remaining 3 patients recovered within one month and experienced brief remissions. This form of therapy merits further trial. It may be considered for use earlier in the course of the disease when there is a smaller total amount of tumor tissue, and thus a greater possibility for its complete eradication. Its use in other neoplastic disorders, as after operative procedures disclosing malignancy, is suggested.

Colimycin and Colimycin-Penicillin Combination in Obstetrics and Gynecology. L. Nobili. Minerva ginec. 11:221-230 (March 31) 1959 (In Italian) [Turin, Italy].

The author reports on the effect of colimycin, an antibiotic derived from Bacillus colistinus, in 12 obstetric patients and in 16 gynecologic patients and on the effect of colimycin combined with penicillin in 7 other gynecologic patients. Each patient received an average of 500,000 units of the drug every 4 hours. The treatment was discontinued if there were no evident signs of improvement, but it was continued for at least 48 hours in patients in whom some regression of the symptoms was obtained. The drug proved to have a good effect on fever, making it disappear within 24 hours to 5 days after the beginning of treatment. The length of treatment (depending on the form of the disease in each patient) ranged from 3 days for 3 patients to 17 days for one patient. The patients received a total dose that varied from 8 million to 38 million units, the drug being well tolerated by all of them. Nineteen of the 28 obstetric and gynecologic patients, 9 with puerperal complications and 10 with gynecologic complications, who had derived no benefit from previous treatment with other antibiotics, had satisfactory results with colimycin. Good results with this drug were also obtained in 7 gynecologic patients with diarrhea, mostly of toxic origin. A marked reduction in the white blood cell count was noticed in some patients, and there was a marked effect on the erythrocyte sedimentation rate in all cases. With the exception of one gynecologic patient, who left the hospital in poor general condition and with fever, colimycin and the colimycin-penicillin combination had a beneficial effect on all the patients.

Use of Methylandrostenediol (Neosteron) in Treatment of Progressive Muscular Dystrophy. G. Bekeny, F. Kraft and S. Lang. Psychiat. et neurol. 137:193-208 (April) 1959 (In German) [Basel, Switzerland].

On the basis of an established relationship between the musculature and testosterone propionate, the male sex hormones have been used in the treatment of disorders of the muscular system. Some of the androgenic steroids produced undesirable virilizing effects, and so efforts were made to synthesize compounds in which these effects would be minimal. One of these, methandriol (Neosteron), which has been in use since 1935, was used by the present authors in the treatment of 30 patients with progressive muscular dystrophy. All the patients were hospitalized, 9 of them twice. The group included 6 female and 24 male patients; 7 of the males were less than 14 years old. For the first 2 or 3 weeks the patients were given the drug by intramuscular injection in daily doses of from 25 to 50 mg. (contained in 1 or 2 cc.). After that the patients continued the treatment at home, taking the drug sublingually. Four of the patients were observed for only 4 weeks. The other patients were under observation for months or even up to 1 or 2 years. No other drug was given simultaneously with methandriol, but some patients received a high protein diet.

The results of treatment are illustrated by case histories. Five patients (4 women and 1 man) obtained great improvement; 18 patients (16 men and 2 women) showed moderate but definite improvement. The remaining 7 male patients, including 3 children, were not improved. The best effects were obtained in the patients who had the recessive, autosomal, ascending (pelvifemoral) type of muscular dystrophy. Patients with the recessive, sex-linked, hereditary, ascending form were less responsive to this treatment. Children with the pseudohypertrophic pelvifemoral form of progressive muscular dystrophy obtained the poorest results. The authors conclude that methandriol produced better results than any other drug. With a daily dose of from 25 to 50 mg., masculinization was

negligible, and no side-effects were observed. Methandriol proved valuable in the treatment of menopausal muscular dystrophy and in polymyositis.

Quinidine Purpura: Report of Six Cases. R. C. Bishop, H. H. Spencer and F. H. Bethell. Ann. Int. Med. **50**:1227-1240 (May) 1959 [Lancaster, Pa.].

This report is concerned with observations on 6 patients in whom thrombocytopenia was associated with the administration of quinidine. The patients were observed at the University of Michigan Hospital and the Simpson Memorial Institute, Ann Arbor, during a period of 50 months. All 6 patients were women, ranging in age from 38 to 69 years. Five of the 6 patients received intermittent quinidine therapy for paroxysmal cardiac arrhythmias. One patient received a single course of quinidine treatment of 3 weeks' duration. Quinidine purpura is not rare, and this diagnosis should be considered in all cases of fulminating bleeding. In cases of suspected quinidine purpura, platelet agglutination tests or other appropriate in vitro studies should be done in an attempt to verify the diagnosis. A diagnostic test dose of quinidine should be given to patients in whom quinidine purpura is suspected only in the presence of negative in vitro tests and with due consideration for the risk to the patient. Treatment of quinidine purpura consists primarily of avoiding further administration of quinidine to the patient. Supportive measures, including blood transfusions, corticotropin (ACTH), and corticosteroids, should be used as the clinical situation dictates.

PATHOLOGY

The Relation of the Pancreatic Ducts to the Islets of Langerhans: Study of Three Cases. Y. H. Yang and W. C. Hunter. A. M. A. Arch. Path. **67**:505-514 (May) 1959 [Chicago].

The authors studied the relation of the pancreatic duct epithelium to the islets of Langerhans in serial sections of pancreatic tissue obtained at autopsy from 3 men, between the ages of 57 and 78 years, who died of coronary arteriosclerosis or of bronchogenic carcinoma. In the case of the first patient a focus of unusual proliferation of pancreatic duct epithelium was found which had an arrangement similar to the islets of Langerhans overlying a capillary network; the individual epithelial cells lacked any granules in their cytoplasm and were small columnar and cuboidal cells with nuclei paler than normal duct epithelium. Serial sections of the pancreas obtained from the other 2 patients revealed quite a few well-formed ducts within the islets of Langerhans as well as direct continuity of minor pancreatic ducts with the islets. These observations offer evidence of transformation of ducts into islet cells by means of proliferation of duct epithelium. The findings further show direct continuity of islet tissue with ducts and establish the histogenesis of the islets of Langerhans from ductal epithelium in adult man. Close relationship of pancreatic duct epithelium with the islets of Langerhans thus exists beyond the embryologic state. Islet cells are capable of further growth or regeneration by new formation from ducts, aside from the division of their own cells. The questions remain: How many islets have direct continuity with ductules in the fully developed human pancreas; how far does this regenerative effort go in restoring the organ to physiological competency, and by what kind of stimuli? Even if there is some connection between the islets and the ductal system, these ducts are not necessarily discharging substances produced by the islets. The authors believe that, while the connection of the islets with the ductal system is present in regenerative states of the islet cells normally, once the islets of Langerhans are fully formed, there is no longer the continuity with the ducts.

Pulmonary Changes in Asian Influenza. P. de Baan. Nederl. tijdschr. geneesk. **103**:721-726 (April 4) 1959 (In Dutch) [Amsterdam].

The author describes the results of studies he carried out on the lungs of 10 patients who died of Asian influenza during the period from October, 1957, to March, 1958. He feels that the unusual character of the pulmonary changes justifies the conclusion that the virus of Asian influenza had invaded not only the bronchial epithelium but also that of the terminal and respiratory bronchioles and of the most peripheral alveoli. The changes consisted of degeneration, necrosis, and desquamation of the epithelium, accompanied by a hemorrhagic and fibrinous exudation in the lungs, and followed by vigorous regeneration of the epithelium at all the aforementioned levels. Thus, the virus of Asian influenza has demonstrated unmistakable signs of pneumotropic properties.

Primary Alveolar Carcinomatosis (Carcinoma) of the Lung (So-called Pulmonary Adenomatosis or Alveolar-Cell Tumour): A Review and Report of 12 Cases. E. Roelsen, T. Lund, T. Søndergaard and others. Acta med. scandinav. **163**:367-384 (no. 5) 1959 (In English) [Stockholm].

Cancer of the lung usually occurs either as a primary bronchiogenic tumor or as metastatic lesions. A third variety is a neoplasm which arises in the respiratory organ itself. During the last 8 years the authors have encountered 12 cases of this special form of pulmonary cancer in a relatively small district in Denmark. The histories of these 12 patients are presented. The first 8 cases are typical of the multiple or diffuse form of primary

alveolar carcinomatosis of the lung, whereas the last 4 are examples of the same histological type of cancer in its solitary form, which has recently been described particularly by Storey and associates. The criteria established by Storey and others for the diagnosis of alveolar cell tumor are (1) a tumor characterized by alveoli lined by epithelial cells of columnal or cuboidal type with eosinophilic cytoplasm and basally placed nuclei, (2) preservation of the pulmonary architecture, (3) absence of an intrinsic tumor of a bronchus, and (4) absence of evidence of primary adenocarcinoma in any other part of the body; these criteria were largely fulfilled by the cases presented. The clinical pictures of the 2 varieties (diffuse and solitary) differed. Dyspnea and cyanosis were predominant in the diffuse variety but rarely present in the solitary form, whereas, with a few exceptions, a productive cough was common to both. Clinically, the most important criterion was the radiographic appearance, which in the diffuse form was highly variegated and difficult of interpretation. Conditions which require differentiation are tuberculosis, sarcoidosis, bronchopneumonia, pneumoconiosis, bronchiectasis, blastomycosis, and coccidioidomycosis. The appearance in the solitary form was less complex, a solitary infiltration or round shadow, but also noncharacteristic.

Only one of the patients with the diffuse form raised abundant amounts of sputum. Cytological studies of the sputum were performed in 8 cases and revealed tumor cells in 5. Bronchoscopy was performed in 3 of the 4 solitary cases, with positive findings in 2. Of the 8 cases of the multiple or diffuse form, 6 were subjected to autopsy, while partial autopsy was performed in 2. The 4 solitary carcinomas were confirmed by histological examination of the specimens removed at operation. It is emphasized that the macroscopic changes, on section, were reminiscent of gray hepatization of lobar pneumonia. Histologically, the alveolar structure was preserved, the alveolar walls being lined with cancer cells. Invasive growth into the lymphatics was common, and metastatic lesions were found in half of the cases. In addition to the alveolar changes, 7 of the patients also revealed changes in the epithelium of the bronchioles. It is likely that this special form of cancer may arise both from the alveolar epithelium and from the bronchioles, and that it may be of either multicentric or unicentric origin.

It is of interest that 8 patients with multiple or diffuse lesions were nonsmokers, while 3 of the 4 patients with solitary lesions were heavy smokers. The prognosis of the multiple or diffuse form was very grave. All 8 patients died within 9 months after the onset of symptoms. The 4 patients with solitary lesions were treated surgically. Two of these are alive, 5 years and 16 months, respectively, after operation. Alveolar carcinomatosis during the years 1949-1956 accounted for 3.5% of all the lung cancer cases notified from the Danish district concerned (population, approximately 500,000). The disease was about equally frequent in both sexes.

Carcinoma and Ulcerative Colitis: A Clinical Pathologic Study: III. Survivors. M. B. Goldgraber, E. M. Humphreys, J. B. Kirsner and W. L. Palmer. Gastroenterology **36**:613-630 (May) 1959 [Baltimore].

In a previous study the authors described 14 cases of carcinoma of the large intestine occurring in patients with ulcerative colitis (abstracted, J. A. M. A. **167**:2148 [Aug. 23] 1958), which group was particularly useful for statistical analysis and comparison with the population at large. This study describes 9 other patients with ulcerative colitis in whom carcinoma of the large intestine developed. All the patients underwent surgical treatment and are currently under clinical observation. The diagnosis of chronic ulcerative colitis was established on the basis of long-standing clinical observation and proctoscopic and roentgenologic findings; that of neoplasm was based on findings obtained from surgical specimens. The average age of the patients at the time of diagnosis of neoplasm was 37 years, with a range of from 19 to 68 years. The average duration of symptoms of ulcerative colitis, before the tumor was diagnosed, was 11.2 years in 8 patients.

Results of the study of these patients indicate that carcinoma of the colon complicating chronic ulcerative colitis occurs at an earlier stage of life than "ordinary" colonic cancer and is more uniformly distributed throughout the colon. It often originates in multiple foci, and presents a wide variety of histological appearances rarely seen in the "usual" cancer of the colon. Pseudopolyps, which were present in most of the patients in this series, seemed to have undergone changes leading to adenoma with atypia. Papillary transformation of the colonic mucosa was a common observation. Nodal involvement did not exclude a long survival.

RADIOLOGY

A Comparison of Techniques for Visualization of the Coronary Arteries. J. I. Fabricant, W. G. Anlyan, G. J. Baylin and R. B. Trumbo. Am. J. Roentgenol. **81**:764-771 (May) 1959 [Springfield, Ill.].

The authors compared various techniques for a safe and reliable method of coronary arteriography in 46 mongrel dogs with myocardial infarcts secondary to ligation of the left anterior descending coronary artery. A base-line coronary arteriogram was taken one week before the ligation of the coronary artery, and a second arteriogram was obtained 2 to 6 weeks after the ligation. The dogs

were then killed, and autopsies were performed 48 hours later. The injection of 30 cc. of a 50% solution of diatrizoate (Hypaque) sodium with an automatic injector through an intra-arterial catheter, with the tip located at the junction of the brachiocephalic artery and the ascending aorta, consistently produced adequate visualization of the coronary arterial tree. The technique was improved by the use of temporary cardiac arrest produced with the injection of 4 to 8 mg. of acetylcholine. Acetylcholine cardioplegia provided a safe, transient asystole; reversion to normal occurred within 2 minutes. Electrocardiographic monitoring, determinations of serum transaminase levels, and histological examinations of the heart carried out at autopsy revealed no significant alterations after induced arrest and arteriography. Because of its alleged capacity for secondary damaging effects, however, the use of Thorotrast (a colloidal solution of thorium dioxide), which provides visualization equally as good as that of diatrizoate, should be restricted.

There apparently is no added hazard in the use of coronary arteriography and acetylcholine cardiac arrest in dogs with myocardial infarcts. Such experimentally induced lesions are depicted clearly. It is proposed that coronary arteriography may be employed as a special diagnostic procedure in the evaluation of patients with coronary occlusive disease. The selection of patients for direct coronary artery surgery, against indirect methods of increasing myocardial blood flow, may be based on such arteriographic studies, which make possible the visual differentiation between diffuse and segmental arterial disease.

Great Vessel Involvement in Lung Cancer: Angiocardiographic Report on 250 Consecutive Proved Cases. I. Steinberg and N. Finby. Am. J. Roentgenol. 81:807-818 (May) 1959 [Springfield, Ill.].

The authors report the results of angiographic studies made on 250 patients with microscopically proved cancer of the lung. Angiocardiography revealed involvement of the superior vena cava system in 31 patients (12%), major pulmonary artery involvement in 46 patients (18%), lobar and segmental pulmonary artery involvement in 131 patients (53.2%), and pericardial invasion in 2 patients (0.8%). No pulmonary vascular changes were revealed by angiocardiography in the remaining 40 patients (16%). The angiographic studies thus disclosed that primary cancer of the lung involved the great vessels (superior vena caval and central pulmonary arterial) in 30% of the patients, therefore making resection impossible. The cases of these patients were chiefly due to hilar and mediastinal involvement. In the 131 patients in whom lobar and segmental pulmonary involvement was revealed by angiography, the latter made possible preoperative evaluation of the cardiovascular system. In some patients, because the vascular deformity was confined to a segment or lobe, lobectomy rather than pneumonectomy seemed feasible. Finally, with bilateral pulmonary disease, angiocardiography provided a precise evaluation of the pulmonary circulation. Thus, pneumonectomy in a potentially respiratory crippled patient was avoided.

For the proper evaluation of the cardiovascular system in patients with cancer of the lung, scrupulous attention to the roentgenographic technique of angiocardiography is essential. Frontal angiocardiograms (taken with the patient in the erect, sitting position) for visualization of the superior vena caval and pulmonary arterial circulation are mandatory. If there is involvement of the main branches of the pulmonary artery, oblique studies are also indicated. The right anterior oblique position should be used when there is deformity of the right pulmonary artery; the left view should be employed when the left pulmonary artery is involved. Then only will angiocardiography achieve its maximum usefulness in determining resectability and prognosis.

Roentgen Signs of Contrast Material Dissection of Aortic Wall in Direct Aortography. D. E. Boblitt, M. M. Figley and E. F. Wolfman Jr. Am. J. Roentgenol. 81:826-834 (May) 1959 [Springfield, Ill.].

The authors report the occurrence of intramural injection of varying amounts of a 70% solution of sodium acetrizoate (Urokon) in 42 of 425 translumbar aortographies performed with the aid of this contrast medium in 390 patients with vascular diseases at the University of Michigan Hospital in Ann Arbor. In 3 instances of the 42, death was either directly or indirectly related to the intramural injection, 2 of the patients dying with proved dissecting aneurysms. The other 39 instances had no significant complications.

The roentgenologic signs of an intramural injection of contrast material are as follows: The cardinal sign is a sharply demarcated, dense collection of contrast medium, showing no evidence of mixing with nonopacified blood. There may be no filling of the aortic branches if the injection is entirely intramural, or a good quality aortogram may be obtained if only a small portion has been deposited in the aortic wall. Should part of the contrast medium dissect back into the aortic lumen or rupture extramurally, a contrast material cast of the aortic wall may persist. If part of the injection is intraluminal, the same phenomenon may be observed as the intraluminal portion is swept downstream. Contrast medium more than a few centimeters above the needle puncture site should arouse one's suspicion concerning an intramural

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injection. If the column is, in addition, sharply demarcated and abnormally dense, one has positive evidence of its intramural location. Additional evidence of an intramural injection is often noted on the delayed roentgenograms. Here one sees the effects of occlusion of aortic branches (either by the intramural injection or the resultant dissecting aneurysm) if contrast medium enters the affected branch before occlusion occurs. The viscus supplied by the occluded branch is persistently opacified by contrast material trapped within it as a result of the loss of normal perfusion pressure.

The importance of the recognition of these signs by everyone performing direct aortography is stressed. The procedure of direct aortography should be discontinued and not attempted again for at least 24 hours if the test roentgenogram shows any evidence of an intramural injection.

The Treatment of Polycythaemia Vera by Irradiation: A Follow-Up Study of 52 Cases. H. D. Friedberg. J. Fac. Radiologists **10**:77-79 (April) 1959 [Bristol, England].

The author reviewed the records of 69 patients in whom polycythemia vera had been diagnosed at the Christie Hospital and Holt Radium Institute in Manchester during the period from 1944 to 1956. This report is concerned with 52 patients, 29 males and 23 females, whose average age was 55 years (range, 24 to 72) when first seen at the hospital. The age at onset of the polycythemia could not be exactly stated, since many patients were vague on this point. Apart from a florid complexion, there were no distinct diagnostic features, and on occasion diagnosis proved very difficult. Often cough and dyspnea were present, and the spleen was frequently palpable. A diagnosis of chronic myeloid leukemia was considered in 15 cases because of a high white blood cell count, but was not substantiated after bone marrow studies. All formed elements of the blood were generally present in excess. The authors show that the term "polycythemia vera" is more apt than the name "erythremia." The chief complication of the disease is the occurrence of intravascular clotting. Thirty-eight thrombotic incidents occurred in 29 patients.

Two radiotherapeutic techniques have been used. In the early period (before 1949) whole-body roentgen irradiation with 250 kv. was used. Since 1949 radiophosphorus (P^{32}) has been used. At first the patient was given 2 or 3 injections of 3 to 5 mc. of P^{32} with intervals of a few months between injections. Now the author gives a single injection of 100 to 140 μc of P^{32} per kilogram of body weight. A total of 20 whole-body irradiations were given to 17 patients, of whom 14 achieved a complete remission (freedom for 6 months or longer from all reversible symptoms). Forty-one P^{32} treatments were given to 28 patients, all of whom obtained remission. Irradiation of the spleen only was tried in 7 patients, but was soon abandoned as the results were not satisfactory. The author concludes that remission can equally well be produced by whole-body roentgen irradiation and by P^{32}. Treatment with P^{32} is simpler; whole-body irradiation is more time-consuming and troublesome.

The Bone Lesions of Childhood Leukemia: A Survey of 140 Cases. J. K. V. Willson. Radiology **72**: 672-681 (May) 1959 [Syracuse, N. Y.].

Since about 1932 it has been the practice at the Harriet Lane Home of the Johns Hopkins Hospital, Baltimore, to include roentgenographic examination of the long bones in the study of children with suspected leukemia. Included in this series are all cases of leukemia seen in the Home, with proof of the diagnosis by blood smear, marrow biopsy, or autopsy, and satisfactory x-ray examinations of the long bones. The age range has been from less than 6 months up to 13 years. Not all the cases of leukemia seen in the clinic are included because often, when the diagnosis is apparent clinically, x-ray examinations are not done. Only suspected cases or cases yet unproved are usually studied roentgenologically. It is this group which largely comprises this series, a total of 140 cases being available for review.

The commonest abnormal findings in this survey of bone lesions was a transverse radiolucent line at the metaphyses of the long bones. Osteolytic destructive lesions and periosteal reaction were also observed. The bone lesions of leukemia were compared with the bone lesions observed in 30 unselected cases of neuroblastoma, which may resemble leukemia radiologically, and with those in 25 cases of rheumatoid arthritis and 20 cases of anemia, which may bear a clinical resemblance to leukemia. The occurrence of a transverse radiolucent line at the metaphyses in diseases other than leukemia was also investigated by a review of 740 consecutive long-bone examinations, comprising all such studies made during one calendar year in the pediatric division of the department of radiology of the Johns Hopkins Hospital. This lesion was observed in 28 patients below the age of 2 years and in 4 patients over that age. The conclusion is offered that the presence of a radiolucent metaphyseal line in a child over the age of 2 years may be of significance in the diagnosis of leukemia. It was not observed in neuroblastoma, rheumatoid arthritis, or the anemias. Below the age of 2 years this lesion may occur in association with many chronic diseases.

The advanced destructive lesions of leukemia present a characteristic pattern, unlike that in other diseases except metastatic neuroblastoma. Clinically, the differential diagnosis from this latter

condition is usually clear. Radiologically, the presence of a transverse radiolucent metaphyseal line associated with destructive lesions is, in general, indicative of leukemia, as this line is not observed in neuroblastoma. When leukemia is suspected, yet unproved, roentgenograms of the long bones should be obtained.

Pleural Effusions Following Supervoltage Radiation for Breast Carcinoma. A. L. Bachman and K. Macken. Radiology **72**:699-709 (May) 1959 [Syracuse, N. Y.].

As long as 200-to-250-kv. roentgen-ray therapy was employed in the treatment of breast carcinoma, either as an adjunct to surgery or for an inoperable lesion, the appearance of a pleural effusion in a patient with carcinoma of the breast has been almost universally considered to indicate metastatic involvement of the pleura and a serious prognosis. In recent years, however, ultra-high-voltage therapy has permitted considerably larger doses to be delivered to the mediastinal, pleural, and parenchymal regions, as well as to the loci of probable disease. As a result, greater radiation effects on the pleura, lung parenchyma, and mediastinal region have been anticipated and, indeed, have already been noted in a number of clinics. At the Francis Delafield Hospital, New York, 2-million-volt radiotherapy has been directed to the breast, axilla, and supraclavicular and internal mammary regions in the treatment of 200 patients, either with inoperable breast carcinoma or postoperatively. Pleural effusions most probably due to irradiation were observed in 11 of these patients.

The authors cite observations that have proved helpful in the differentiation between effusions resulting from irradiation and from metastases. Effusions due to irradiation always appeared within 6 months after completion of radiotherapy, often within 2 to 4 months. Such an effusion was accompanied by radiation pneumonitis, and spontaneous disappearance of the fluid indicated that it was probably due to irradiation. In cases in which the fluid had disappeared, or remained stationary in amount, for considerable periods of time and then rather suddenly reappeared or increased in amount, the cause of the reaccumulation was found to be metastases. However, the radiographic appearance and persistence of the effusions were not found to be significantly helpful in differentiating the 2 conditions. In both groups the fluid was found either loculated or in the free pleural cavity, and in both the effusions were observed to persist more or less unchanged in amount for long periods of time. The relationship of the radiation effusions to conventional and supervoltage radiotherapy, total dose delivered, and radiation pneumonitis is discussed.

PHYSIOLOGY

The Physiologic Basis for Vasopressor Therapy During Shock. S. E. Greisman. Ann. Int. Med. **50**:1092-1114 (May) 1959 [Lancaster, Pa.].

The therapeutic usefulness of vasopressor agents remains highly controversial. Some investigators disapprove of their indiscriminate use; others advocate such therapy routinely. Those who recommend routine employment of vasopressor therapy often fail to consider the following conditions: 1. Improvement of the systemic arterial blood pressure is not synonymous with therapeutic benefit. 2. Lessening of cyanosis, though generally a favorable sign, actually may connote further tissue ischemia, rather than improved blood flow. 3. The survival of a previously healthy young male treated with vasopressor agents and the death of an elderly, emaciated male without such therapy do not prove the value of the therapy. 4. The difficulty in evaluation of the severity of shock leads to inaccuracy in appraisal of any form of therapy. 5. Studies which fail to identify the precipitating factor and the duration of shock are virtually meaningless, since the precipitating factor and the time factor determine the potential value of vasopressor drugs. 6. Certain supplemental forms of treatment may influence the outcome of shock.

Rather than attempt to determine the efficacy of vasopressor therapy from the numerous uncontrolled clinical reports, the author considers the mechanisms of action of vasopressor drugs in relation to certain physiological derangements of the peripheral vascular system during the various shock syndromes. The ability of the normal animal to maintain an adequate systemic arterial blood pressure despite a blood volume considerably smaller than the capacity of the vascular bed depends in part upon physiological control by peripheral vasomotion. This vasomotor process is a dual system. Capillary vasomotor activity comprises the first line of defense, and arteriolar vasomotion represents the second line, preventing blood from entering, distending, and pooling within the capillary reservoir. During the early phase of low blood volume shock, both the capillary apparatus and the arteriolar vasomotor apparatus exhibit an intensification of constrictor activity. At this stage the capillary system is highly responsive to vasopressor agents. As shock progresses, the capillary vasomotor process, at least in the mesenteric area, undergoes progressive impairment and becomes increasingly refractory to vasopressor agents, whereas arteriolar constriction is maintained by neurogenic control enhanced by humoral factor activity.

The fundamental derangement underlying this impairment of capillary vasomotion appears to reside in tissue ischemia. Sustained arteriolar constriction is an important contributing factor. Although arteriolar constriction serves as an imme-

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diate lifesaving mechanism during rapid and severe blood loss, the resultant ischemia in certain tissues (of which the intestine seems to be especially important) hastens the impairment of capillary vasomotor function and the progression to irreversible shock. Hypoxia, release of products of anaerobic tissue metabolism, and absorption of bacterial endotoxins probably contribute significantly. The mechanisms of action of vasopressor and antipressor agents during experimental shock have been reviewed. Until data from controlled studies are obtained on the action of vasopressor agents during human shock, it is suggested that vasopressor therapy be reserved for specific clinical situations.

Residual Neurohypophyseal Function in Hypophysectomized Man. J. F. Dingman, A. G. Jessiman, R. H. Despointes and others. New England J. Med. 260:997-1001 (May 14) 1959 [Boston].

The authors report on 16 patients treated by hypophysectomy for metastatic cancer of the breast. The operation was performed by a transfrontal approach. In the first 2 patients operated on, the infundibular stalk was divided in its midportion, the proximal stump was cauterized, and a silver clip was applied. In both patients severe polyuria occurred, requiring constant vasopression therapy. In the third patient, removal of a metastatic tumor in the vicinity of the sella turcica required the application of a silver clip to the cut end of the stalk. Permanent diabetes insipidus occurred postoperatively in the patient. The surgical technique was modified in the remaining 13 patients in that the infundibular stalk was severed close to the diaphragma sellae ("low section") and its proximal portion gently retracted without cauterization or application of clips. Moderate to pronounced polyuria was evident during the immediate postoperative period in 12 of the 13 patients, but pronounced polyuria persisted in only 1. In an attempt to clarify the role of the pituitary gland in the undesirable complication of diabetes insipidus, residual neurohypophyseal function was evaluated at least 3 weeks after operation in the 16 patients by measurement of the antidiuretic response to nicotine or hypertonic sodium chloride solution administered intravenously, when permanent postoperative levels of water excretion had become established. The degree of neurohypophyseal insufficiency and resultant diabetes insipidus was directly associated with injury of the infundibular stalk incurred at surgery, and was significantly lessened by careful neurosurgical techniques aimed at preserving hypothalamic neurosecretory function.

Diabetes insipidus continued unabated, despite discontinued administration of cortisone, in patients devoid of neurohypophyseal function. Low rates of free water excretion were observed in patients possessing residual neurohypophyseal activity. The degree of polyuria bore little relation to osmolal or creatinine clearances. The conclusion is drawn that the functional integrity of residual neurohypophyseal tissue in the hypothalamus plays an important part in regulating the excretion of solute-free water in patients with combined anterior and posterior pituitary insufficiency.

PUBLIC HEALTH

Vaccinations Against Adenovirus Infections: Observations in Schools for Recruits in Switzerland in 1958. O. Gsell and H. Mäder. Schweiz. med. Wchnschr. 89:315-320 (March 21) 1959 (In German) [Basel, Switzerland].

The authors review the history of studies on the adenovirus infections, pointing out that this group of viruses was discovered by 2 groups of investigators in disorders referred to by such terms as "adeno-pharyngeal-conjunctival fever," "acute respiratory illness," and "adenoid degeneration." These viruses produce an excess of lactic acid, are localized in the cell nucleus, and can be demonstrated in the form of basophil inclusions. They are resistant to certain antibiotics and ether and are thermolabile and filtrable. They have a common, soluble, complement-fixing group-antigen, and by means of neutralization tests with immune serums, they can be differentiated into types, 18 human serotypes having been identified. Infections with the adenoviruses have been observed in many countries in recent years; in fact, if a search is made by virologic or serologic tests, it is found that they are rather common.

Because of recurrent epidemics, particularly among military recruits, vaccines were first prepared and tried in the United States. A 5-valent vaccine (types 1, 3, 4, 5, and 7) was used in 3 schools for recruits in Switzerland in the spring of 1958. In each school half of the recruits were vaccinated by a single intramuscular injection of 1 cc. of the vaccine. All of the 589 recruits tolerated this injection without untoward reactions. Since no adenovirus infections occurred in these military schools, it is difficult to evaluate the efficacy of the vaccine. Asian influenza developed just as frequently in the vaccinated as in the unvaccinated. Complement-fixation tests demonstrated that antibodies against adenoviruses were present 15 days after the vaccination, but after 3½ months they could no longer be detected. The authors conclude that vaccination with polyvalent adenovirus vaccine can be recommended for young adults in military service and for children in camps, since a considerable number of adenovirus infections may thus be prevented. For other persons, however, this form of vaccination is not indicated because of the low index of infection and the mild course of the infections.

BOOK REVIEWS

Hypnosis in Modern Medicine. Edited by Jerome M. Schneck, A.B., M.D., Clinical Associate Professor of Psychiatry, State University of New York College of Medicine, New York City. Second edition. Cloth. $8.75. Pp. 389. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The statement on the dust jacket of this edition reads, "Completely revised and set from new type." Except for the quality of the paper, a page-by-page comparison of the two editions discloses them to be identical, even with regard to the typographical errors (pages 30, 213, and 216). There has been no revision, and a revision was needed. For example, 9 of the 11 chapter bibliographies are alphabetically arranged for the reader's benefit. Two are in scrambled order and these two, as well as several others, have numerous items of questionable value or pertinence. Grantly Dick-Read's name is abused in the text, in two bibliographies, and even in the index, as is that of Anthony Owen-Flood. In the bibliography for his own chapter, the editor evidently considered 16 of his papers "in press" and two "to be published" sufficiently important references to be listed in the first edition, but not of sufficient importance to warrant giving the actual references as to date and place of publication in the second edition six years later. Actually, one of these references, 101, was published the year before the first edition, but it is still listed as "in press" in this second edition.

In his preface to the second edition, the editor declares, "it seems wise in this second edition to retain the original form and content and to supplement the basic structure of the book with the latest significant data. To achieve this aim, a review of the literature has been organized and appended. Emphasis has been placed upon clinical advances. The basic chapters on history and instruction have not, therefore, been enlarged." One wonders whether this last is meant to imply that the other chapters were enlarged. Examination of this new appended review of the literature in the book discloses approximately 40 full pages of text divided among 11 sections, covering such topics as internal medicine, psychiatry, psychophysiology, and theory. In these few pages, "to supplement the basic structure of the book with the latest significant data," what purports to be a general discussion and summary of publications for the period 1953-1959 is offered. However, of the total bibliography of 151 items listed for this new part (psychological abstracts lists between 350 and 400 references for the same period of time), 30 are the editor's own writings, 24 antedate the first edition of the book, only 9 are as recent as 1957, only 26 as recent as 1956, and there are none for 1958. In brief, the book is not a revised edition, nor does it contain, as the editor asserts, the "latest significant data."

Whatever merit this second edition has derives, then, almost entirely from that of the first edition. As for the book itself, it is a symposium of uneven quality, with 11 contributors. There is considerable unnecessary overlapping which the editor could have corrected. Six of the chapters are of excellent quality, five are no more than fair. Considering the latter first, these are the chapters on hypnosis in internal medicine, in surgery, in anesthesiology, in obstetrics and gynecology, and in child psychiatry. The chapter on internal medicine is an interesting but discursive account of a little of everything from urology to psychiatry and is marred by an effort at poetic prose. The 87-item bibliography includes a simple listing of general textbooks on psychiatry, psychoanalysis, neurology, and orthopedic surgery.

Hypnosis in Surgery might better have been entitled "psychiatric problems sometimes encountered in relation to surgery." As an article on the latter subject it is reasonably good, but little information about hypnosis in surgery is given. The 41-item bibliography has too many general references. Also, those references listed as "in press" in 1953 have not been corrected by the editor of the "new edition." The 12-page chapter on anesthesiology is decidedly poor, uninformative, and expresses too many dogmatic opinions; the nine-item bibliography is without value, and the author's name is listed both correctly and incorrectly in the indexes of both editions.

The chapter on obstetrics and gynecology demonstrates that the author writes well, is widely read, but is content in this instance to give his readers only a general account, richly interlarded with references to associated and even remotely related matters. The nonalphabetical 82-item bibliography contains many irrelevant listings. Of definitely poor quality is the chapter on hypnosis in child psychiatry. It is essentially an inadequate account of such practice before 1900, with some scattered brief current material. The 28-item bibliography is also lacking in value.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

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Unlike the chapters just mentioned, the initial chapter of the book, History of Medical Hypnosis, is a pleasure to read and delightfully informative. An excellent 42-item bibliography is given. Hypnosis in Dermatology is a thought-provoking, stimulating, informative chapter of significant value to any reader, whatever his field of competence, because of the explication of hypnosis as a methodology. The 59-item bibliography is also excellent.

The editor's chapter on Hypnosis in Psychiatry is also of excellent quality: comprehensive, informative, and well organized, it is only slightly marred by his ready emphasis on his own writing, at the expense of more extensive studies in the literature which he merely cites as references. His bibliography of 152 items is, on the whole, good despite the fact that of the 41 references to his own work, 18 of these are listed in both editions as not yet published.

The chapter on Hypnosis in Dentistry is delightfully comprehensive and thoroughly informative. It bespeaks a background of extensive understanding and experience over a long period of time and the material is presented simply and directly. Unfortunately, the 28-item bibliography is too general to be of much value. Physiologic Aspects of Hypnosis is an outstanding contribution, thoroughly well organized and presented, constituting a competent survey of the literature, with a well-selected 119-item bibliography.

The final chapter, Instruction in Hypnosis, presents adequately and informatively the understandings one needs in teaching hypnosis, the problems to be encountered, and the special understandings that must be given to the role that patients as individuals must necessarily play in the use of hypnosis. Briefly then, this is a book dating back to 1953, not a new 1959 edition as claimed, and over half of it is good, in fact, very good.

Hypertension: The First Hahnemann Symposium on Hypertensive Disease. Edited by John H. Moyer, M.D., Professor and Chairman of Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia. With assistance of John R. Beem, M.D., and others. Cloth. $14. Pp. 790, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

In this report of a symposium held in Philadelphia by a large group of expert clinicians and research workers in the field, the emphasis is on the clinical aspects of hypertension. The book is divided into sections on the pathology and clinical aspects of hypertension, on basic concepts of etiology, on pharmacology, on the role of salt and diuretics, and on surgery. Each section is followed by verbatim reports of the discussion.

Most readers have mixed feelings about books of this sort. They seem to be necessary lest anyone think symposia cater only to the selected few. On the other hand, one must admit that few readers have the time or patience to digest so great an amount of disorganized talk; only reviewers are required to do so. This book contains a vast amount of information and an equally vast amount of contradictory material. Those inexpert in the field would find it hard to know just what is a correct, or even the prevailing, view. Probably the book is an accurate reflection of the actual confusion in many of the contributors' minds.

Since there were 91 contributors to the symposium, it is impossible to give even a sampling of the content. It appears that the usefulness of books such as these could be immeasurably increased by liberal use of the editor's shears. This is an unpopular suggestion, but what reader has the time to unscramble a blow-by-blow description of a conference? In addition, the discussions are loaded with the "slide-in-the-pocket" technique which strains the patience of the reader even more than that of the audience.

On the other hand, it must be clearly stated that much solid information is contained in this book. It is altogether suitable for those who have an uncommon interest in reading the barometer of the field. Such readers will be well repaid for their effort because these pressures are nowhere better registered. To them this book is heartily recommended, with thanks to Moyer and his group for the effort.

International Textbook of Allergy. Edited by J. M. Jamar, M.D., Lecturer at University of Louvain, Louvain. Cloth. $17.50. Pp. 639, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada; Ejnar Munksgaard, Nørregade 6, Copenhagen, K, Denmark, 1959.

The 25 chapters of this book were written by 31 contributors: 6 from the United States, 2 from Canada, 1 from Argentina, 1 from Brazil, and the other 21 from various European countries. The book is well written in excellent English, a tribute to the editing of J. M. Jamar of Brussels. Only occasionally does an awkward phrase suggest that English is not the native language of most of the authors. Each chapter is an essay on a special subject and is followed by a fairly comprehensive list of references.

The book has two sections, a short one of 65 pages on fundamental subjects and a long one of 574 pages on clinical allergy. The first is well written, despite the limited space assigned and contains chapters entitled Anaphylaxis, Physiopathological Role of Histamine in Man, and Allergy and Immunology. The last chapter is a particularly concise, clear statement of present knowledge in this field.

The second section, composed of clinical material, varies in quality from excellent to poor. Four out of five chapters on asthma are in the first category;

Pathophysiology of Bronchial Asthma, Clinical Aspects of Bronchial Asthma, Specific Treatment of Bronchial Asthma, and Status Asthmaticus summarize adequately our present knowledge of the subject. Other well written chapters include The Clinical Use of Corticotropin and Adrenocortical Steroids, Vascular Allergy and Collagen Diseases, Allergy and Hematology and, finally, Reactions to Drugs.

Some of the other chapters, despite the distinction of their authors, are either inadequate or of variable quality. For instance, the description of methods of therapy or of diagnostic procedures with little or no distinction between obsolete and currently accepted practices tends to mislead the uninitiated reader. The use of nonspecific fever therapy for asthma is mentioned without critical evaluation. Occasionally theories are stated as if they were established facts, e. g., the otherwise stimulating chapter on Alimentary and Gastrointestinal Allergy, which mentions pathogenic and saprophytic organisms and intestinal parasites and micro-organisms found in other organs as possible causes of intestinal allergy. This statement is made without supporting evidence and reference to published work.

It is understandable that uniformity of quality is difficult to achieve in an "international textbook" on allergy. Dr. Jamar's volume is, on the whole, a successful approach to the goal. Presumably it is intended for the advanced reader and worker in allergy rather than for the beginner.

The Demonstration Clinic for the Psychological Study and Treatment of Mother and Child in Medical Practice. By David M. Levy, M.D., Clinical Professor of Psychiatry, Columbia University, New York. With preface by Leona Baumgartner, M.D. Cloth. $5. Pp. 120. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

This book provides a most readable illustration of the way in which psychological understanding by the physician can be used for the study and treatment of the emotional life of the children seen in a child health center. The use of verbatim recordings of interviews is an invaluable tool for the teaching of psychological interviewing techniques.

Dr. Leona Baumgartner says in the introduction (page vii) that perhaps one of the reasons the "demonstration clinic" has been so widely accepted is that the project has been built on the existing skills and attitudes of the doctors. It has emphasized the physiological approach, without attempting to give the physicians a long period of "psychiatric orientation." This is perhaps one of the pitfalls of the program. Psychiatry has discovered and organized a certain body of knowledge which is essential for understanding child behavior and development. Without this basic knowledge the physicians in these interviews are likely to have given patients false information, and they may have minimized psychological problems which need more attention.

The superficiality of some of the theories maintained by the physicians is indicated in case 4, footnote 4, on page 66. "Nailbiting as a possible result of a deficit in previous biting or chewing activity is considered. In that manner it would follow the same principle of causation as in finger sucking which in most instances is proof of a deficiency in sucking activity." This physician recommends giving children wooden sticks to bite as treatment for nailbiting and also recommends putting adhesive tape on thumbs of thumb suckers, so that the pressure will not cause displacement of the teeth. Both the explanation given and the treatment recommended are completely inadequate and psychologically naïve.

Without the footnotes it would be difficult to understand why the doctor interrupts or minimizes a problem the mother has brought up. However, one frequently feels that the physician has not followed through with the mother's initial complaint. The interviews are rushed and necessarily inadequate. The reader is confused throughout by the double focus of the interview. On the one hand it is to offer help to the mother. On the other hand there are frequent references to the fact that the doctors are observing and learning norms of behavior and physical development for their own benefit. These two emphases often interfere with each other. Part of the difficulty in maintaining the continuity of the interview is that the psychiatrist and the pediatrician are thinking of their relationship to each other as well as their relationship with the mother. For example, on page 19 occurs the remark, "It is interesting" with the explanation that this statement was "half" directed to the physician. Its purpose is partly to keep the physician inside the interview, to reduce the tension of repeated questioning, and also to facilitate the mother's response by imparting the feeling that she is contributing to our knowledge. It is doubtful whether the mother's response is facilitated when she feels she is contributing to the physician's knowledge. On the other hand, this feeling may inhibit her in presenting problems that are of real concern to her.

In case 2 the problem of the conflict between mother and grandmother was handled very well. The attempt to use the mother's own resources for solving her problems deserves special emphasis. In case 3 the physicians recognized the need for social services for the family, such as specific psychiatric casework therapy for the temper tantrums and hyperactivity of the 3½-year-old child.

This book is a valuable contribution toward the psychological study and treatment of patients in medical settings. Persons interested in public health and welfare are likely to find this book helpful and stimulating. More such studies are needed.

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QUESTIONS AND ANSWERS

EXPOSURE OF CHILD TO SUN

To the Editor:—*I am interested in knowing the effect of exposure of infants to sun rays. Specifically, is it beneficial? How long should an infant between 4 and 11 months of age be exposed? Is any particular protection suggested?*

P. C. Corrado, M. D., New York.

Answer.—It is well established that sun rays are beneficial to an infant in providing a natural source of vitamin D, which is essential for normal bone growth and development. It has been well documented for more than 50 years that children swathed in cloth and kept in the dark develop rickets with regularity in contrast to those infants allowed to have normal skin exposure to the ultraviolet rays of the sun. The amount of exposure in the age limits mentioned would depend on the extent of natural pigmentation of the skin. A blond, fair-skinned baby would require less exposure than would a dark-skinned child. It has been shown that exposures of 15 to 30 minutes a day are more than adequate to prevent rickets in infants. Protection to prevent excessive burning from the actinic rays would include adequate clothing for most of the surface of the body. A small hat to shade the eyes and face would be advisable also.

EVALUATION OF PSYCHOTHERAPY

To the Editor:—*Has anyone ever done a good double-blind study to evaluate psychotherapy? That is, has a sufficiently large group of patients, some of whom had therapy and some of whom had not, ever been evaluated by a disinterested group of psychiatrists before and after (if there was therapy) to determine how many were helped and how many were made worse by psychotherapy or by the lack of it?*

Robert M. Fisher, M.D., Rosemont, Pa.

Answer.—No good double-blind studies to evaluate psychotherapy have as yet been devised, chiefly because of the difficulty in accurately defining and assessing what is meant by therapeutic change. However, fine efforts have been made to investigate these problems of adequately controlling psychotherapy for scientific evaluation of results of outcome of treatment. Many difficulties arise in matching groups of patients and assessing nontherapeutic factors which might produce change. For example, it has recently been hypothesized that a significant "placebo" effect may result from the patient's conviction that psychotherapy is helping him. Since it is nearly impossible to conceive of "inert" psychotherapy, it is exceedingly difficult to separate the placebo effect from the essential effect of the treatment. Again, it is difficult to evaluate environmental factors adequately for matching groups, and it would be impossible to hold these factors constant throughout the research. Thus far, one way to avoid the matched-group requirement is to have each patient serve as his own control in a "wait" period before therapy. Still, there is no way of controlling environmental influence in different time periods.

Control problems are further complicated by ethical demands. For example, can the investigator ethically withhold treatment to satisfy his scientific curiosity? Furthermore, in recent years it has been the vogue to use more sophisticated statistical techniques along with a more clearly formulated research design. Statistical devices such as analysis of co-variants may be used to introduce "controls" that matching often cannot provide. Effective use of such statistical tools, however, requires that the relevant variables be identified just as they must be in the conventional control approach, and this requirement has been a sizable stumbling block in clinical research. The variables are so many and so frequently hard to measure that it is next to impossible to identify the "important" case. Occasionally a hitherto totally disregarded factor turns out to be the one that discriminates "improved" and "unimproved" patients, perhaps, and doubt is immediately cast on other studies in which this factor is neither controlled nor randomized.

Reznikoff and Toomey, in their book "Evaluation of Changes Associated with Psychiatric Treatment," reviewed the investigations of the Menninger Foundation group, C. R. Rogers and associates, and Watson and Mensh. The work of these groups seems to represent the best studied and documented projects thus far.

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Reznikoff, M., and Toomey, L.: Evaluation of Changes Associated with Psychiatric Treatment, Springfield, Ill., Charles C Thomas, Publisher, to be published.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

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APHTHOUS STOMATITIS

To the Editor:—*I have under treatment a patient, aged 32, with intractable aphthous stomatitis. I read recently that nystatin has given surprisingly good results. Please advise on the value of that preparation.*

Carlos Lozano De Lamo, M.D.
Cartagena, Spain.

Answer.—The causes of aphthous stomatitis are unknown, but apparently secondary invasion by micro-organisms generally found in the mouth plays a role in continuation of the process. Therefore, in some cases, relief can be brought about by the use of appropriate antibiotics. Nystatin powder, or lozenges containing this antibiotic, will prove of value in some cases in combating secondary infection with Candida. In other cases, powdered tetracyclines will prove valuable as mouthwashes (Distelheim and Sulzberger, *J. Invest. Derm.* 13:115, 1949) when secondary invasion by cocci and other micro-organisms sensitive to the tetracyclines has occurred. Recently, a preparation derived from Lactobacillus acidophilus and L. bulgaricus has been reported to give excellent results in relieving the pain and shortening the duration of the ulcers. This is dissolved in milk and used as a mouthwash.

In some cases, recurrences are brought on by exposure to allergens such as nuts, shellfish, pork, and chocolate. In others, trauma to the mucous membrane apparently initiates the attack. In these patients, careful avoidance of the offending type of exposure may result in long periods of freedom. Despite all of these palliative measures, many recurrent cases resist all forms of treatment.

TETANUS IMMUNE GLOBULIN

To the Editor:—*I would appreciate advice regarding administration of tetanus immune globulin to a horse serum–sensitive patient with a tetanus-prone injury. I am obliged to desensitize a large number of such individuals. The induced serum antitoxin titer (0.03 units per cubic centimeter) is less than the minimum required (0.10 per cubic centimeter). However, supposedly this product still gives better protection because of its human gamma globulin content.*

J. J. Kraut, M.D., Los Angeles.

Answer.—Administration of the commonly used tetanus antitoxin made with horse serum to a patient who is horse serum–sensitive but has a tetanus-prone injury is fraught with the danger of an anaphylactic reaction. Formerly, an antitoxin which was not prepared in the horse, as for example bovine tetanus antitoxin (containing cow serum), was substituted, but the latter serum was not always available and had to be given in much larger amounts than the equine type. Tetanus immune globulin would seem to be advantageous in this particular situation; even though the antitoxin content may be somewhat less than the required minimum, this can be obviated in badly infected wounds by administering larger amounts of the globulin. The product containing human globulin has the advantages of persisting in the tissues for longer periods than horse serum antitoxin and also of not inducing a delayed serum reaction, which can occur after bovine antitoxin administration. However, it should be remembered that both preparations (the serum or the globulin) confer only a temporary passive immunity, lasting perhaps several weeks after their administration. Active immunity can be induced only by injecting the toxin itself, as contained in tetanus toxoid. Regardless of which product is used, the effect is not one of "desensitization," as mentioned by the inquirer, but of neutralization of the toxin. If the tetanus globulin is given, the individual, if prone to injury, still should be actively immunized later by a course of injections of tetanus toxoid.

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VACCINATION AGAINST TUBERCULOSIS

To the Editor:—*I desire information on vaccination against tuberculosis. The province in which I practice is about 70 miles square and has a population probably between 600,000 and 1 million. There is some bone and lymph gland tuberculosis and much pulmonary tuberculosis. What company sells BCG vaccine? What procedure is recommended for doing the vaccinations? What age group should be vaccinated? Is it necessary to do skin tests before vaccination? Will BCG reduce all types of tuberculosis or only pulmonary? What results can be hoped for from BCG vaccination?*

Nathan J. Barlow, M.D.
Soddo, Wollamo, Ethiopia.

Answer.—Some 40 years ago in the United States it was common to have a large percentage of clinic and institutional patients with glandular tuberculosis, as well as many thousands with bone tuberculosis. Today, these are a rarity. The improvement can be credited largely to the fact that in 1916 the U. S. Public Health Service ordered the tuberculin testing of all cattle and the destruction of those found diseased. BCG can be obtained from the Institute of Tuberculosis Research, University of Illinois College of Medicine, 1853 W. Polk St., Chicago, Ill. Full directions for its proper use will be sent. BCG is an attenuated vaccine of tubercle bacilli which acts to create a sensitization to such bacilli in the absence of previous infection. It is

therefore necessary to determine the presence of existent infection by tuberculin testing. Positive reactors should not be given BCG. The incidence of infection increases from birth on into adolescence and adult life. It is therefore important to vaccinate as soon after birth as possible, as well as to make certain there is no contact with individuals having open tuberculosis. The big battle is to control and eliminate open infection.

INDUCTION OF LABOR

To THE EDITOR:—*The question of the safety of inducing labor with six doses of 1 minim (0.062 cc.) of pituitary extract at half-hour intervals with only a nurse in attendance has come before the staff. Some nurses do not want to give it unless the attending physician is present in the building. What is advised?*

O. E. Torkelson, M.D., Lusk, Wyo.

ANSWER.—There is wide variation in sensitivity of the uterus to oxytocic drugs in different individuals. Every safeguard must be employed in use of these potent physiological agents to prevent undesirable sequelae to mother and baby. The pure oxytocic principle of posterior pituitary, either natural or synthetic, should always be used. Extracts containing pressor and antidiuretic factors have no place in obstetrics. The safest procedure for induction of labor at term is an intravenous drip consisting of 10 units of the oxytocic in 1,000 cc. of 5% dextrose. The rate of administration should be 8 or 10 drops a minute until uterine response is observed. Initiation of rhythmic contractions and intervals of relaxation should follow in a short time. The frequency of contractions, their duration, and absence of alteration in the fetal heart pattern should determine the speed with which the drip may be increased. Ideally, a physician should be in attendance; at least, he should be readily available while a competent person is observing the patient. Administration of oxytocic drugs for the induction of labor by other than intravenous drip will increase the hazards to mother and baby.

CYTOTHERAPY IN MONGOLISM

To THE EDITOR:—*Does cytotherapy with fresh or desiccated cells taken from various organs of animal fetuses (such as pigs and calves) have any effect on diseases such as Mongolism? Is such treatment generally approved? Is there any indication for it?*

H. B. Madeno, M.D., Monterrey, Mexico.

ANSWER.—There are protagonists of replacement therapy for Mongolism, but most physicians would consider such attempts foredoomed to failure. Mongolism is a constellation of congenital cerebral, ocular, cardiac, and other somatic defects, of such nature that they are hardly alterable by endocrine, vitamin, or antibiotic therapy. This is not to say that life expectancy has not increased on a modern therapeutic regimen. The danger is that mothers of these defective infants will generally place an illusory hope on the use of cytotherapy or any other kind of specific therapy. Vitamins, iron, thyroid substance, glutamic acid, and other dietary or replacement measures have all had their day. However, the intricate anatomic features of this form of mental retardation, with the minute deformities of skull, heart, fingers, eyes, and brain that characterize Mongoloid anomalies and which are already present at birth, make it exceedingly unlikely that a "cure" will ever be found. The possibilities of antenatal prevention seem more likely.

INDICATIONS FOR HYSTERECTOMY

To THE EDITOR:—*What are the correct treatments for the various atypical cellular changes found in the uterine cervix? By these I mean squamous metaplasia, atypical hyperplasia of varying degree, basal cell hyperplasia, and other changes, excluding carcinoma in situ and true carcinoma. Would hysterectomy be advisable for any of these patients? If so, which? Should a repeated biopsy show a change from, say, mild atypical hyperplasia to severe atypical hyperplasia, would that be a reason for hysterectomy?*

M.D., Louisiana.

ANSWER:—Treatment of cervical lesions is influenced by a number of factors, including age of the individual, extent of the lesion, severity of symptoms, and associated disease within the pelvis (such as prolapse, relaxation, or myomas). Inflammatory lesions of the cervix may produce considerable changes in epithelium on and in the cervix. Metaplasia is not necessarily in itself particularly significant. It depends on the extent and type of metaplasia. On the other hand, the cervical cells may extend out to the vaginal portion, or squamous cells may extend up through the cervical canal.

Excluding carcinoma in situ and true carcinoma, hysterectomy would not be the recommended or routine treatment procedure. Hysterectomy is a major procedure not required by the conditions mentioned. Comparisons of biopsy specimens with earlier ones is important. For an individual who shows abnormal cellular structure at or near the menopause, there would be less criticism of hysterectomy, especially if there were other conditions present for which hysterectomy could be a part of the treatment. For a woman in the late 20's or early 30's, only marked tissue changes would justify hysterectomy.

UNEXPLAINED FEVER

To the Editor: *A female, aged 7, has had intermittent attacks of abdominal pain, fever, headache, nausea, and vomiting for the past 18 months. Sedimentation rates have been normal. Intravenous pyelogram and gallbladder, barium enema, and upper gastrointestinal studies have been normal. On several hospital admissions, blood cell counts and urinalyses were essentially normal, as were stool examinations. Exploratory laparotomy revealed many adhesions around the gallbladder which were thought to be infectious in origin. The appendix was removed and reported normal by the pathologist. The child made an uneventful recovery but has had recent recurrence of abdominal pain, fever, nausea, and vomiting. Further physical examination does not contribute anything toward a diagnosis. There are numerous enlarged cervical lymph nodes. Three siblings are well.*

M.D., Pueblo, Colo.

Answer.—The causes of indeterminate fever are numerous. It is very important to know about the degree of fever and whether it is episodic or continuous. Among common conditions that should be considered are retroperitoneal inflammatory lymph nodes, lymphoma, regional enteritis, and the presence of parasites in the stool. It should be possible to settle the problem of inflammatory nodes or lymphoma by removing some of the nodes for pathological examination. It is sometimes difficult to establish the diagnosis of regional enteritis by gross inspection of the intestine, particularly in early cases. Presence of parasites can be ruled out only by repeated stool examinations.

VOICE CHANGE AND SINGING

To the Editor:—*Should a boy whose voice has started changing be stopped from singing? Some chorus teachers let them keep on in spite of the probable strain on their voices. On the basis of my training in laryngology I would not allow any singing at all.*

M.D., South Carolina.

Answer.—This question has been a matter of disputation for many generations. According to Brodnitz (Keep Your Voice Healthy: Guide to Intelligent Use and Care of Speaking and Singing Voice, New York, Harper & Brothers, 1953), Manuel Garcia, who gave to medicine the laryngeal mirror and opened a new era in the study of the human voice, fought for complete voice rest, in contrast to Dr. Morel Mackenzie, who in 1888 wrote the first scientific book on the hygiene of the vocal organs and believed that easy exercises would be helpful in the transition. Most experts apparently agree that choir singing, the prevalent form of singing at that age, with its lack of individual control, is harmful. Schubert and Haydn are supposed to have lost their voices that way. Serious vocal studies should not be begun in boys before 18 to 19 years of age and in girls before 17.

LIQUID TO REMOVE WARTS

To the Editor:—*What is the name of the liquid preparation prescribed to remove warts and moles?*

G. Howard Wood, M.D., Chillicothe, Ohio.

Answer.—Many liquid preparations are used to remove warts, but chemicals are not considered good treatment for any type of "mole." All warts are benign, with practically no danger of malignant change ensuing from such treatment even if long-continued. However, moles comprise a large group of nevic conditions, several types of which may terminate as carcinoma or melanoma. To treat a mole with such potentialities with irritating chemicals is dangerous. A biopsy is frequently necessary to differentiate one type of mole from the other. Since this is the case, and since most moles are small, complete surgical removal is the logical procedure. Chemicals that may be used in the treatment of warts are trichlor or monochlor acetic acid, diacetic acid, salicylic acid, sulfuric acid, nitric acid, podophyllin, liquid nitrogen, and formaldehyde. Some of these preparations have been incorporated in collodion for application.

HEMANGIOMATOSIS

To the Editor:—*Is there any medicinal or other nonsurgical means for controlling hemorrhage from intestinal lesions of hemangiomatosis (Rendu-Osler-Weber disease)?*

John F. Hardham, M.D., Paso Robles, Calif.

Answer.—There is no evidence that medicinal or other nonsurgical methods of therapy can have any effect on the bleeding from intestinal lesions of hemangiomatosis. There have been some reports that hormone therapy, either estrogens or combinations of estrogens and androgens, may be effective, but there are no good data available, and one must remember that hemorrhagic states are characterized by subsidence of bleeding spontaneously. Therefore, whatever agent is used at the time may receive unwarranted credit. It has been noted that removal of telangiectatic lesions from the intestinal tract, especially the small intestine, frequently is followed by occurrence of more lesions in adjoining areas. These patients should be given iron and may at times need transfusions. Fatal hemorrhages are very uncommon, and therefore maintenance therapy may keep such patients in fairly good condition.

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